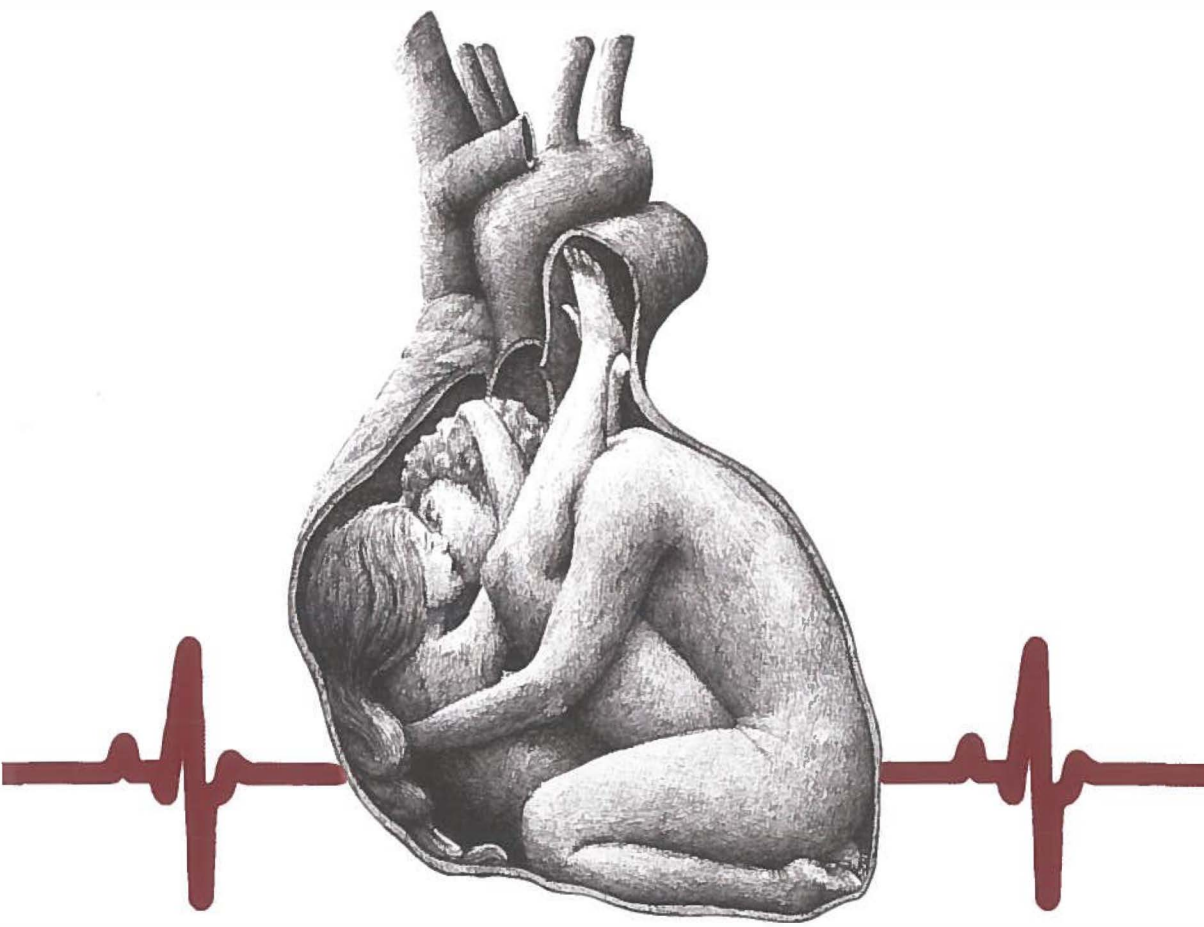
Quality of life and sexual problems in patients with heart failure

Hoekstra, Tialda

Quality of life and sexual problems in patients with heart failure



Tialda Hoekstra

Quality of life and sexual problems in patients with heart failure

Tialda Hoekstra

Financial support by the Netherlands Heart Foundation and the Groningen University Institute for Drug Exploration (GUIDE) for publication of this thesis is gratefully acknowledged.

The research described in this thesis was supported by grants of the Netherlands Heart Foundation (2000Z003 and 081201/K&I/RW/DM)

ISBN 978-90-367-5794-2
ISBN electronic version 978-90-367-5795-9

Cover	Illustration	Redmer Hoekstra, www.redmerhoekstra.nl
	Design	Wietske Hooghiemstra
Lay out		Tialda Hoekstra
Printed by		Grafimedia, Facilitair bedrijf RUG

Stellingen

behorende bij het proefschrift

Quality of life and sexual problems in patients with heart failure

door
Tialda Hoekstra

1. Het verbeteren van het fysiek functioneren bij patiënten met hartfalen leidt niet alleen tot een betere kwaliteit van leven, maar ook tot een kleinere kans op het hebben van seksuele problemen en overlijden. *(Dit proefschrift)*

2. In tegenstelling tot wat de huidige literatuur doet vermoeden, zijn het niet alleen de mannen met hartfalen die seksuele problemen ervaren. *(Dit proefschrift)*

3. De seksuele behoefte van patiënten met hartfalen is een taboe. *(Dit proefschrift)*

4. Zolang patiënten denken dat hartfalen de veroorzaker is van hun seksuele problemen, dienen hulpverleners seksualiteit met hen te bespreken, ongeacht of de veronderstelling klopt. *(Dit proefschrift)*

5. Een vergelijkbaar slechte kwaliteit van leven is één van de weinige overeenkomsten tussen patiënten met hartfalen en een behouden en een verminderde linker ventrikel ejectie fractie. *(Dit proefschrift)*

6. Brain natriuretische peptide (BNP) als marker voor de ernst van hartfalen is bij patiënten met hartfalen en een behouden linker ventrikel ejectie fractie discutabel. *(Dit proefschrift)*

7. Een stelling is gemakkelijker te weerleggen dan op te stellen. *(Aristoteles)*

8. Naast sport, zouden werkgevers ook muziek maken en toneel spelen bij hun werknemers moeten stimuleren om de kans op burn-out te verlagen.

9. Resultaten op de golfbaan zijn gerelateerd aan zowel het fysiek als het emotioneel functioneren van de golfer.

10. Accepteren is meer dan ja zeggen.

11. Het verdient aanbeveling te onderzoeken hoe het mogelijk is dat veel mensen, die gewoon twee oren en één mond hebben, toch functioneren alsof die verhouding net andersom is.

12. Met de huidige bezuinigingen op wetenschappelijk onderzoek dreigen universitaire werkzaamheden te verschuiven van onderzoeken naar wonderzoeken.

rijksuniversiteit groningen

Quality of life and sexual problems in patients with heart failure

Proefschrift

ter verkrijging van het doctoraat in de
Medische Wetenschappen
aan de Rijksuniversiteit Groningen
op gezag van de
Rector Magnificus, dr. E. Sterken,
in het openbaar te verdedigen op
maandag 10 december 2012
om 11.00 uur

door

Tialda Hoekstra

geboren op 23 november 1979
te Heerenveen

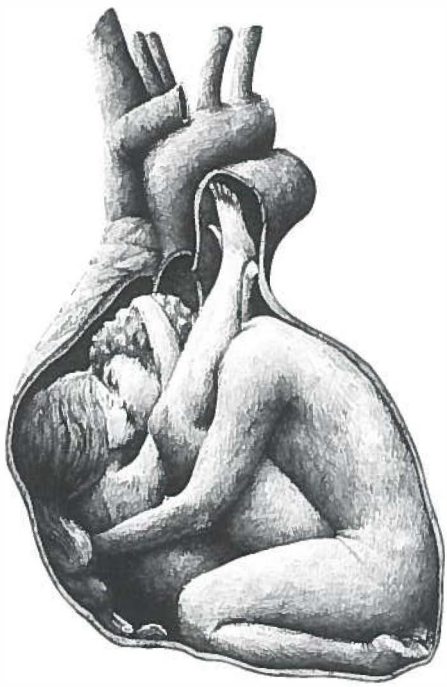
Promotores:	Prof. dr. D.J. van Veldhuisen
	Prof. dr. T. Jaarsma
	Prof. dr. R. Sanderman
Copromotor:	Dr. I. Lesman-Leegte
Beoordelingscommissie:	Prof. dr. A.V. Ranchor
	Prof. dr. J.W.M.G. Widdershoven
	Prof. dr. H.B.M. van de Wiel

Paranimfen: Maurice M.W. Nieuwenhuis
Johan H. Pijlman

The publication of this thesis was financially supported by Rijksuniversiteit Groningen, Universitair Medisch Centrum Groningen, MSD, Menarini Farma Nederland, St. Jude Medical Nederland B.V., Novartis Pharma B.V.

Contents

Chapter 1:
Introduction and aims of the thesis



Introduction and aims of the thesis

Current research on (non)pharmacological therapies and devices for patients with heart failure has shown that such measures are effective in decreasing mortality and readmission rates. Success in prolonging survival in combination with increased aging of the general population, will lead to a dramatic increase in the prevalence of patients living with heart failure.[1] Although patients live longer nowadays, heart failure strongly affects the quality of their lives, which is worse compared with healthy elderly subjects, the general population, and patients suffering from other chronic disorders.[2-4] In recent years, patient preferences and patient centred outcomes, such as quality of life, have become of greater importance, particularly because life expectancies for patients with heart failure have increased. Consequently, patients have to adjust to living with a chronic condition. It is interesting to note that for many (elderly) patients, quality of life appears to be more important than longer survival.[1,5] Fortunately, improving quality of life is recognized as one of the major treatment goals in the heart failure guidelines of the European Society of Cardiology.[1] Although this recognition has resulted in an increase in studies on quality of life of patients with heart failure, there are still many gaps in this research area. For example, there is limited knowledge of the quality of life of patients with heart failure and a preserved ejection fraction (HF-PEF). Sexual health, which forms an important component of quality of life of both men and women with cardiovascular disease, has also received little attention.[6] This thesis intends to address these gaps, and has two aims: firstly, to gain more insight in the quality of life of patients with heart failure, specifically in patients with HF-PEF, and secondly, to address the sexual health of patients with heart failure.

Chronic heart failure: definition and epidemiology

Heart failure is generally defined as the inability of the heart to supply sufficient blood flow to meet the needs of the body and organs. Heart failure is a chronic disease which has the following features: shortness of breath at rest or during exertion; fatigue; signs of fluid retention such as pulmonary congestion or ankle

swelling; and objective evidence of an abnormality of the structure or function of the heart at rest.[1]

The most common causes of functional deterioration of the heart are damage to the heart muscle or loss of the heart muscle's ability to contract, acute or chronic ischemia, increased vascular resistance with hypertension, or the development of a tachyarrhythmia such as atrial fibrillation. Coronary heart disease is by far the most common cause of myocardial disease, being the initiating cause in about 70% of the patients with heart failure.[7,8]

Heart failure is one of the most prevalent chronic diseases worldwide, affecting between 2 to 3% of the general population. It is even more frequently present in the elderly, with a prevalence of 10-20% in people aged 70 years or older.[1] In 2007, in the Netherlands an average of 6.2 out of a 1000 males, and 8.5 out of a 1000 females were diagnosed with heart failure. In patients aged 85 years or older, the prevalence was even higher: 33.6 per 1000 males, and 40.9 per 1000 females.[9] The overall prevalence of heart failure has increased dramatically over the past decades, due to a combination of increased aging of the general population, the successful increase in survival in patients suffering from coronary events, and the success in postponing coronary events by implementing effective prevention measures for those at high risk or those who survived a first coronary event.[7,10]

In the past, within the heart failure patient population a distinction was frequently made between systolic heart failure and diastolic heart failure. Nowadays, the terms heart failure with reduced left ventricular ejection fraction (HF-REF) and heart failure with preserved ejection fraction (HF-PEF) are more regularly used for both patient populations. Patients with HF-PEF have symptoms and/or signs of heart failure and a preserved left ventricular ejection fraction (LVEF) of >40-50%. Patients with HF-REF have an LVEF of <40%.[1] Population-based epidemiology prevalence studies suggest that almost half of the patients with heart failure have HF-PEF.[11,12] Compared with patients with HF-REF, HF-PEF patients are more often older, female, obese, and suffering from diabetes.[11] Due to the presence of these co-morbidities, it is often difficult to diagnose heart failure. In fact, some patients with assumed HF-PEF do not have heart failure, but suffer

from another condition, such as anaemia, lung disease, or depression.[11,12] To account for this difficulty, the guidelines of the European Society of Cardiology now state that untreated patients with symptoms of heart failure should have plasma levels of B-type natriuretic peptide (BNP) of at least 100pg/ml to confirm the diagnosis of heart failure.[1] The inclusion of this criterion in the guidelines may be a first step to make the diagnosis of HF-PEF easier, and to differentiate between patients with heart failure and patients with other conditions. For instance, due to the implementation of this guideline, patients with heart failure symptoms, a preserved ejection fraction and BNP levels <100pg/ml no longer meet the HF diagnostic criteria, but rather appear to suffer from another condition.

With respect to BNP levels, it is often assumed that the prevalence of co-morbidities among patients with low BNP levels is higher than in patients with high BNP levels. However, besides their low BNP levels, it is not known how these patients differ from patients with HF-PEF and BNP levels >100pg/ml, nor is it known how they should be diagnosed and treated.

Quality of life in patients with heart failure

The World Health Organisation (WHO) has defined quality of life as 'individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns'.[13] The WHO also states that 'it is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment'.[13] Although there has been some debate on the methods of measuring health-related quality of life, an international group of quality of life experts has reached agreement upon health-related quality of life assessments. Four dimensions are fundamental to any health-related quality of life measure; these include physical, mental/psychological, and social health, as well as global perceptions of functioning and well-being. Furthermore, the experts agreed that the primary source for health-related quality of life assessment should always

be the study participants, or the patients.[14] In this thesis, the words 'quality of life' are used when 'health-related quality of life' is meant. Apart from the dimensions of quality of life, all aspects are considered together when patients are asked to rate 'their overall quality of life' or 'overall well-being'.

In a quality of life assessment a variety of different instruments can be used, measuring different components of health. Disease-specific instruments, for example, measure symptoms that are specific to the disease being studied, or the consequences of the disease on participants' quality of life. These instruments are sensitive to subtle disease-specific changes. A disease-specific instrument that is often used in heart failure studies is the Minnesota Living with Heart Failure questionnaire.[15] Disease-generic instruments, on the other hand, measure the overall functioning or satisfaction with each area of life, independent of the specific disease of the patient. The quality of life of patients in a particular study can then be compared with the quality of life of patients with other diseases, such as COPD or diabetes. In our study we used the RAND 36-Item Health Survey and Cantril's Ladder of Life to measure disease generic quality of life.[16,17]

Heart failure has a major impact on the physical, mental, and social domains of the quality of life of patients.[1,18] Patients with heart failure have a significantly lower quality of life than age- and gender matched members of the community.[2] Compared with other chronically ill patients, the psychical and mental health of patients with heart failure is often equally, of even more so, impaired.[4] Although it is known that heart failure has a negative impact on the length and quality of life of patients,[19] studies on whether quality of life in itself has a prognostic power with respect to the prediction of mortality are inconsistent.[20] Some studies have found an association between poorer quality of life and lower survival rates. However, inconsistencies may arise from the usage of a limited number or different quality of life instruments, and from the variety of follow-up periods, ranging from a couple of months till several years.[20] Furthermore, it not only remains unclear which quality of life dimensions predict mortality best, and in order to reduce mortality, which patient-related factors are associated with these dimensions.

Nowadays, in the heart failure guidelines, improving quality of life is recognized as one of the major treatment goals.[1] However, the majority of studies on improving treatment outcomes and quality of life have been conducted in patients with HF-REF. There is only limited knowledge of the quality of life of patients with HF-PEF compared with patients with HF-REF. This is remarkable, especially considering the fact that about 50% of all patients with heart failure have HF-PEF.[11,12] Therefore, it is important to study the quality of life of patients with HF-PEF.

Sexual problems in patients with heart failure

Besides suffering from symptoms that include fatigue and shortness of breath, patients with heart failure also have to cope with psychological factors, such as depression, low functional capacity, and the need to manage lifestyle changes.[2,21-25] These factors not only affect their overall quality of life, but also their intimacy needs.[26] Although it is often assumed that sexual activity is not important for seriously ill patients, patients with heart failure do consider sexual activity in their current condition as an essential aspect of quality of life. Unfortunately, symptoms of heart failure affect the sexual relationships of these patients.[6,27,28] At least 50% of all patients with heart failure report their sexual activity has decreased or even completely ceased as a result of their heart failure. Furthermore, half of the patients have problems with sexual activity caused by erectile dysfunction or orgasmic problems, and experience sexual dissatisfaction.[26-29] Previous research has mainly focused on male sexuality and erectile dysfunction.[27] However, heart failure symptoms like dyspnoea, fatigue, and exercise intolerance can also be assumed to affect the sexual health of both male and female patients. Considering the demographical characteristics of patients with heart failure in daily practice, in which 50% is female and 30-50% is living alone, more in-depth information is needed on the problems of both female and male patients.[30-32]

At the same time it should not be forgotten that there are age- related changes in sexuality, caused by normal hormonal changes, vascular damage, or muscular weakness, that are independent of heart failure. This means sexual problems might

be part of the aging process and therefore not only caused by heart failure.[33] For further research on this subject it is important to have insight in the nature and cause of sexual problems of patients with heart failure compared with healthy members of the community.

Although the current heart failure guidelines recommend counselling on sexual activity to both male and female patients and their partners, previous studies have shown that even though healthcare providers do feel responsible for discussing sexual health, they rarely discuss this topic with their patients in practice.[1,29,34] To improve patient care, it is important to know which barriers withhold healthcare providers, in particular nurses, from discussing this issue with their patients. Heart failure nurses are becoming more and more involved in the long-term management of patients with heart failure, and it can be expected that they have an increasingly important role to play in discussing sexual health and the consequences of heart failure on sexual health with patients and their partners.

Aims of this thesis

To gain more insight in the quality of life and the sexual health of patients with heart failure, the following aims of this thesis are formulated:

- To examine the prognostic value of quality of life on long-term survival of patients with heart failure.
- To examine the quality of life of patients with a preserved left ventricular ejection fraction in more detail.
- To assess the prevalence of sexual problems and related factors in patients with heart failure.
- To describe the current practice of discussing sexuality by heart failure nurses.

To accomplish the first three aims, data from the COACH study (Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure) are used. COACH was a multicenter, randomized clinical trial on the effect of a disease management program in heart failure.[35, 36] A total of 1023 patients from 17

hospitals in the Netherlands were enrolled in the COACH study. Patients were included in the study during a hospitalization for heart failure (NYHA functional class II to IV), with heart failure as the primary diagnosis. During hospitalization all patients received standard care, both pharmacological and non-pharmacological, according to the guidelines.[1] After the baseline assessment, patients were randomised to either 'care-as-usual', basic support, or intensive support, which differed in the intensity of advising and counselling provided. Follow-up assessments took place at 1, 6, 12 and 18, months after discharge.

The first aim of this thesis is addressed by examining the predictive value of three different quality of life instruments (general well-being, disease-generic quality of life and disease-specific quality of life), on long-term mortality (Chapter 2).

Chapter 3 addresses the quality of life of patients with HF-PEF compared with patients with HF-REF. Chapter 4 specifically focuses on the quality of life of patients with HF-PEF, and will compare patients with low BNP levels and high BNP levels.

Chapters 5 and 6 focus on the third aim. In Chapter 5, the prevalence of sexual problems is examined by using one question on sexual functioning from the Minnesota Living With Heart Failure questionnaire. Patients who perceive problems are compared with patients who do not perceive problems on a broad range of characteristics and quality of life dimensions. Chapter 6 covers the specific problems patients with and without a partner experience with sexuality due to their heart failure, compared with healthy community controls. This chapter also addresses the differences between younger and older patients with respect to sexuality.

Finally, in Chapter 7 the current practice of discussing sexual health and the perceived responsibility of heart failure nurses for addressing this topic are described, as are the barriers that prevent them from discussing sexuality with their patients.

Recommendations for clinical practice and future research to improve quality of life in patients with heart failure, including discussing sexual health, will be described in Chapter 8.

References

1. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. *Eur J Heart Fail* 2008;**10**:933-989.
2. Lesman-Leegte I, Jaarsma T, Coyne JC, et al. Quality of life and depressive symptoms in the elderly: a comparison between patients with heart failure and age- and gender-matched community controls. *J Card Fail* 2009;**15**:17-23.
3. van Jaarsveld CH, Ranchor AV, Kempen GIJM, et al. Gender-specific risk factors of mortality associated with incident coronary heart diseas: a prospective community-based study. *Prev Med* 2006;**43**:361-367.
4. Juenger J, Schellberg D, Kraemer S, et al. Health related quality of life in patients with congestive heart failure: comparison with other chronic diseases and relation to functional variables. *Heart* 2002;**87**:235-241.
5. Jaarsma T, Beattie JM, Ryder M, et al. Palliative care in heart failure: a position statement from the palliative care workshop of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2009;**11**:433-443.
6. Lindau ST, Schumm LP, Laumann EO, Levinson W, O'Muircheartaigh CA, Waite LJ. A study of sexuality and health among older adults in the United States. *N Engl J Med* 2007;**357**:762-774.
7. Murdoch DR, Love MP, Robb SD, et al. Importance of heart failure as a cause of death. Cahnging contribution to overall mortality and coronary heart disease mortaility in Scotland 1979-1992. *Eur Heart J* 1998;**19**:1829-1835.
8. Fox KF, Coewie MR, Wood DA, Coats AJ, Gibbs JS, Underwood SR. Coronary artery disease as the cause of incident in heart failure in the population. *Eur Heart J* 2001;**22**:228-236.

9. Gommer AM, Poos MJJC. *Cijfers coronaire hartziekten (prevalentie, incidentie en sterfte) uit de VTV 2010*. In: Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid. Bilthoven: RIVM; 2010.
10. Senni M, Tribouilloy CM, Rodeheffer RJ, et al. Congestive heart failure in the community: trends in incidence and survival in a 10-year period. *Arch Intern Med* 1999;**159**:29-34.
11. Kindermann M, Reil JC, Pieske B, et al. Heart failure with normal left ventricular ejection fraction: what is the evidence? *Trends Cardiovasc Med* 2008;**18**:280-292.
12. Paulus WJ, van Ballegoij JJ. Treatment of heart failure with normal ejection fraction: an inconvenient truth! *J Am Coll Cardiol* 2010;**55**:526-537.
13. Kuyken, on behalf of the WHOQOL Group. The World Health Organisation Quality of Life assessment (WHOQOL): position paper from the World Health Organisation. *Soc Sci Med* 1995;**41**:1403-1409.
14. Berzon R, Hays RD, Shumaker SA. International use, applications and performance of health-related quality of life instruments. *Qual Life Res* 1993;**2**:367-368.
15. Rector TS, Kubo SH, Cohn JN. Patients' self-assessment of their congestive heart failure: content, reliability and validity of a new measure, the Minnesota Living with Heart Failure questionnaire. *Heart Failure* 1987;**3**:198–209.
16. Cantril H. *The pattern of human concerns*. New Brunswick, NJ: Rutgers University Press; 1965.
17. Van der Zee KI, Sanderman R, Heyink JW, de Haes H. Psychometric qualities of the RAND 36-item Health Survey 1.0: a multidimensional measure of general health status. *Int J Behav Med* 1996;**3**:104-122.
18. Lesman-Leegte I, van Veldhuisen DJ, Hillege HL, et al. Depressive symptoms and outcomes in patients with heart failure: data from the COACH study. *Eur J Heart Fail* 2009;**11**:1202-1207.

19. van Veldhuisen DJ, Cohen-Solal A, Böhm M, et al. Beta-blockade with nebivolol in elderly heart failure patients with impaired and preserved left ventricular ejection fraction. *J Am Coll Cardiol* 2009;**53**:2150-2158.
20. Mommersteeg PM, Denollet J, Spertus JA, Pedersen SS. Health status as a risk factor in cardiovascular disease: a systematic review of current evidence. *Am Heart J* 2009;**15**:208-218.
21. Jaarsma T, Halfens R, Abu-Saad HH, et al. Quality of life in older patients with systolic and diastolic heart failure. *Eur J Heart Fail* 1999;**1**:151-160.
22. Jaarsma T, Lesman-Leegte I, Hillege HL, et al. Depression and the usefulness of a disease management program in heart failure: insights from the COACH (Coordinating study evaluating Outcomes of Advising and Counseling in Heart failure) study. *J Am Coll Cardiol* 2010;**55**:1837-1843.
23. Smart N, Haluska B, Jeffriess L, et al. Exercise training in systolic and diastolic dysfunction: effects on cardiac function, functional capacity, and quality of life. *Am Heart J* 2007;**153**:530-536.
24. Winkelmann ER, Chiappa GR, Lima CO, et al. Addition of inspiratory muscle training to aerobic training improves cardiorespiratory responses to exercise in patients with heart failure and inspiratory muscle weakness. *Am Heart J* 2009;**158**:768.e1-7.
25. Van der Wal MH, Jaarsma T, van Veldhuisen DJ. Non-compliance in patients with heart failure; how can we manage it? *Eur J Heart Fail* 2005;**7**:5-17.
26. Jaarsma T, Dracup K, Walden J, et al. Sexual function in patients with advanced heart failure. *Heart Lung* 1996;**25**:262-270.
27. Schwarz ER, Kapur V, Bionat S, et al. The prevalence and clinical relevance of sexual dysfunctioning in women and men with chronic heart failure. *Int J Impot Res* 2008;**20**:85-91.
28. Jaarsma T. Sexual problems in heart failure patients. *Eur J Cardiovasc Nurs* 2002;**1**:61-67.

29. Westlake C, Dracup K, Walden JA, et al. Sexuality op patients with advanced heart failure and their spouses or partners. *J Heart Lung Transplant* 1999;**18**:1133-1138.
30. Cleland JG, Swedberg K, Follath F, et al. The EuroHeart Failure survey programme--a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis. *Eur Heart J* 2003;**24**:442-463.
31. Heo S, Moser DK, Chung ML, et al. Social status, health-related quality of life, and event-free survival in patients with heart failure. *Eur J Cardiovasc Nurs* 2012;**11**:141-149.
32. Gallagher R, Luttik ML, Jaarsma T. Social support and self-care in heart failure. *J Cardiovasc Nurs* 2011;**26**:439-445.
33. Wylie K, Kenney G. Sexual dysfunction and the ageing male. *Maturitas* 2010;**65**:23-27.
34. Gott M. Hinchliff S. Barriers to seeking treatment for sexual problems in primary care: a qualitative study with older people. *Fam Pract* 2003;**20**:690-695.
35. Jaarsma T, Van Der Wal MH, Hogenhuis J, et al. Design and methodology of the COACH study: a multicenter randomised Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure. *Eur J Heart Fail* 2004;**6**:227-233.
36. Jaarsma T, van der Wal MH, Lesman-Leegte I, et al.; Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH) Investigaters. Effect of moderate or intensive disease management program on outcome in patients with heart failure: Coordinating Study Evaluating Outcomes of Advising and Counselling in Heart Failure (COACH). *Arch Intern Med* 2008;**168**:316-324.

Chapter 2:
Quality of life and survival in patients with heart failure

Tialda Hoekstra, Tiny Jaarsma, Dirk J. van Veldhuisen, Hans L. Hillege, Robbert Sanderman, Ivonne Lesman-Leegte

European Journal of Heart Failure 2012; Accepted for publication

Abstract

Aims: To examine whether self-rated disease specific and generic quality of life predicts long-term mortality, independent of brain natriuretic peptide (BNP) levels, and to explore factors related to low quality of life, in a well-defined heart failure (HF) population.

Methods: A cohort of 661 patients (62% male; age 71; left ventricular ejection fraction 34%) was followed prospectively for 3 years. Quality of life questionnaires (Ladder of life, RAND36 and Minnesota living with Heart Failure Questionnaire) and BNP levels were assessed at discharge after a hospital admission for HF.

Results: Three-year mortality was 42%. After adjustment for demographic variables, clinical variables and BNP levels, poor quality of life scores predicted higher mortality; per 10 units on the physical functioning (hazard ratio (HR) 1.08; 95% confidence interval (CI) 1.02-1.14), and general health (HR 1.08; 95% CI 1.01-1.16) dimensions of the RAND36. Patients with low scores on these dimensions were more likely to be in New York Heart Association class III-IV, diagnosed with co-morbidities, have suffered longer from HF, have lower estimated glomerular filtration rates, and had fewer beta-blocker prescriptions.

Conclusion: Quality of life was independently related with survival in a cohort of hospitalized patients with HF.

1. Introduction

Heart failure (HF) has a negative impact on the length and quality of life (QoL) of patients.[1,2] Studies on whether QoL in itself has prognostic power for the prediction of mortality are inconsistent. Some, but not all, studies have found an association between poorer QoL and worse survival.[3] Inconsistencies in previous studies may be explained by their using different QoL instruments to predict outcomes. Most studies used one questionnaire, or focused on one subscale or question from a specific QoL questionnaire. Only a few have used disease-generic QoL questionnaires (Short Form-36 (SF-36)) simultaneously with disease-specific QoL questionnaires (Minnesota Living with Heart Failure questionnaire (MLwHFQ), Kansas City Cardiomyopathy Questionnaire) in their patient population to describe the association between QoL and survival in HF patients.[3] Inconsistencies may also arise from the different follow-up periods used in the different studies, which ranged from a couple of months to >5 years, and each study adjusted for different demographic and clinical variables.[4-8] The majority of studies did adjust for disease severity by using left ventricular ejection fraction (LVEF) or the New York Heart Association (NYHA) functional class.[3] However, both NYHA and LVEF have limitations as markers for disease severity. LVEF only reflects the severity of LV systolic dysfunction and not the severity of HF,[9] whereas NYHA classification is highly subjective based on the endurance of the patient and is directly associated with (physical) QoL. Furthermore, the utility of NYHA classification used as a marker of disease severity is currently the subject of some debate owing to low inter-rater reliability.[10] Brain natriuretic peptide (BNP) has in recent years emerged as a reliable reflection of the severity of HF.[11] None of the aforementioned studies used BNP as a marker for the severity of HF.

Provided that QoL is a predictor of mortality, the important next step is to find out which patients have a low QoL. In order to reduce mortality, these patients in particular could benefit most from additional treatment, focused on improving QoL.

To gain more insight into the prognostic value of QoL, we examined the predictive value of several QoL instruments for long-term mortality in a large

group of HF patients. In order to control with an objective parameter for the severity of HF, we adjusted for plasma levels of BNP in our analyses. Additionally, we examined the characteristics of patients with high and low QoL scores.

2. Methods

2.1 Patient population

Data were collected as part of the COACH study (Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure). COACH was a multicentre, randomized clinical trial on the effect of a disease management programme in HF, the design, main results and first QoL data have been published.[2,12-14] In brief, 1023 patients from 17 hospitals in The Netherlands were enrolled in the COACH study. Patients were included in the study during a hospitalization for HF (NYHA functional class II-IV), with HF as the primary diagnosis. The diagnosis was based on a combination of typical signs and symptoms according to the European Society of Cardiology (ESC) guidelines[15] for which a hospital stay was considered necessary. During hospitalization all patients received standard care, both pharmacological and non-pharmacological, according to the guidelines,[15] in a cardiology ward, staffed by cardiologists and registered nurses. Patients were 18 years or older and had evidence of structural underlying heart disease. Exclusion criteria were: concurrent inclusion in a study requiring additional visits to research healthcare personnel; restrictions that made the patient unable to fill in data collection forms; an invasive intervention within the last 6 months or planned during the following 3 months; or ongoing evaluation for heart transplantation. All patients gave written informed consent.

The Central Ethics Committee approved the study protocol and the extended 3-year follow-up data collection on survival. The study was performed in accordance with the principles outlined in the Declaration of Helsinki.

2.2 Data collection

Plasma BNP levels were determined once and analysed locally within 4h of blood collection (1 mL of blood, collected in EDTA), on the day of hospital discharge or on the day before hospital discharge. All BNP measurements were performed using a fluorescence immunoassay kit (Triage®; Biosite Incorporated, San Diego, CA, USA).[16] Data on left ventricular function were obtained by standard transthoracic echocardiography.

Survival data were collected during the 18-month follow-up period of the COACH study as part of the primary endpoint of the study. Cause of death and the date of the event were adjudicated by a central end-points committee. Concerning the patients who survived the 18-month follow-up period, 3-year follow-up (1095 days) data on all-cause mortality were collected from the hospital registry, and the general practitioner and/or municipality, 3 years after the last patients was included in the COACH study. For each patient who survived the initial 18-month follow-up, but died afterwards, a calculation was made on the time period between dying and inclusion in the COACH study in order to have an equally long follow-up period for each patient (1095 days).

Data on QoL were collected during hospitalization. Quality of life was assessed in three different ways: global well-being, disease-generic QoL and disease-specific QoL.

Global well-being was assessed by Cantril's Ladder of Life. This is a single-item measure which asks the patient to rate their sense of well-being on a ladder, with 10 reflecting the best possible life imaginable and 0 reflecting the worst possible life imaginable. Cantril's Ladder of Life has been used in various cardiovascular studies and is considered to be a valid measure of global well-being.[17] A higher score indicates better well-being.[18]

Disease-generic QoL was assessed by the Medical Outcome Study 36-item General Health Survey (RAND36), a self-report questionnaire of general health status and comparable with the Short-Form-36 Health Survey (SF-36).[19,20] The RAND36 is a well-validated generic, 36-item questionnaire that includes nine health concepts that represent dimensions of QoL: physical functioning, social

functioning, role limitations because of physical functioning, role limitations because of emotional functioning, mental health, vitality, bodily pain, general health and perceived health change. Each dimension has a score between 0 and 100; a higher score means better health.[19]

Disease-specific QoL was measured with the Minnesota Living with Heart Failure questionnaire (MLwHFQ).[21] The MLwHFQ is a 21-item scale, with a scoring range of zero for no impairment, to 105 for maximum impairment as a result of HF. Three scores can be determined: a total score (21 items, 0-105), the physical dimension (8 items, 0-40), and the emotional dimension (5 items, 0-25). Higher scores mean a worse QoL. The questions cover symptoms and signs relevant to HF, e.g. physical activity, social interaction, sexual activity, work and emotions. All patients were instructed by trained data collectors to report if, and to what extent HF has affected their life during the last month on each item. The reliability and validity of the MLwHFQ have been documented.[21]

2.3 Statistical analysis

Descriptive statistics were used to characterize the study population. Data are presented as means ± standard deviations (SDs) or percentages. Student's t-tests and Mann-Whitney tests for continuous variables and Chi^2 square tests for categorical variables were performed to compare demographic characteristics, clinical characteristics and QoL between patients who survived and did not survive the 3-year follow-up period. Cox proportional hazards regression was used to determine the independent association of QoL with time to mortality. Separate analyses were made for each scale: the nine dimensions of the RAND36, both subscales and total score of the MLwHFQ and the Ladder of Life. To evaluate a possible effect-modifying role of potential risk factors with regard to mortality, three Cox regression analyses were performed; first including the QoL scale, secondly adjusting for age and gender, and finally adjusting for all variables with a theoretical or univariate association with mortality (p-value <0.10 two tailed). Within the third model there was no hierarchical inclusion of the variables. All variables were entered as dummies except for age, BNP, QoL scales, systolic

blood pressure, diastolic blood pressure, heart rate, sodium, and estimated glomerular filtration rate (eGFR) which were modelled as continuous variables. The RAND36 dimensions and the total score of the MLwHFQ were recoded per 10 units. To gain hazard ratios (HRs) >1.00 for reasons of readability, the scores of the RAND36 dimensions per 10 units and the Ladder of Life scores were subtracted from 10. All QoL scales were stratified by centre.

More in-depth analyses on patient characteristics of the two QoL dimensions with the highest prediction on survival were performed. We compared patients who scored in the lowest quartiles with patients who scored in the highest quartiles on these dimensions. Kaplan-Meier curves with a log-rank test were constructed for the patients in the lowest and highest quartiles of both dimensions. Statistical significance was set at two-tailed $p<0.05$. Analyses were performed with STATA version 11 (StataCorp., College Station, TX, USA).

3. Results

3.1 Patient characteristics

Of the 1023 patients included in the main COACH study, a BNP-level was available in 766 patients. Within the patient sample of 766 patients, all QoL questionnaires at baseline were completed by 661 patients (86%). Only patients with available BNP levels who completed all questionnaires were included in the current study. Patients who were excluded from the current study did not differ from the study sample on age, gender, NYHA functional class at discharge, and LVEF function.

Patients had a mean age of 71 years (± 11), 61% was male and 40% were living alone. The mean LVEF was 34% (± 14), 33% had an LVEF >40%, and at discharge 51% were classified as NYHA functional class III-IV (Table 1). During the 3-year follow-up, 276 (42%) patients died; no patients were lost to follow-up. Patients who died during the follow-up period were significantly older, more often in NYHA III-IV, had higher BNP levels at hospital discharge, lower systolic and diastolic blood pressure, lower eGFRs, had been diagnosed with HF for longer,

were more often previously hospitalized for HF, and were more often diagnosed with diabetes or had a stroke in the past than patients who survived the 3-year follow-up period. Furthermore, the survivors were more often treated with angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs) and beta-blockers at discharge than the non-survivors (Table 1).

3.2 Quality of life

Global well-being at baseline, as measured with Cantril's Ladder of Life, did not differ significantly between survivors and non-survivors (6.3 (± 1.7) vs. 6.2 (± 1.9), p=0.170).

Mean scores of all dimensions of the RAND36 in the total group varied between 18 and 66 on the theoretical range between 0 and 100, with the lowest scores for role limitations physical (18 (± 33)), health change (25 (± 23)), and physical functioning (34 (± 26)). Non-survivors had a significantly lower QoL at baseline than survivors on the physical functioning (28 (± 23) vs. 39 (± 27), p<0.001), role limitations physical (13 (± 27) vs. 22 (± 36), p<0.001), bodily pain (60 (± 34) vs. 66 (± 34), p=0.031) and general health (41 ± 18 vs. 46 ± 19, p=0.001) dimensions (Figure 1).

The mean score in the total group on the total scale of the MLwHFQ was 44 (±21). On the physical and emotional subscales, mean scores were 24 ± 23 and 7.1 ± 6.1, respectively. On the MLwHFQ non-survivors rated their QoL at baseline significantly lower than survivors on the total score (47 (± 19) vs. 42 (± 22), p=0.010) and the physical subscale (25 (± 9) vs. 22 (± 11), p=0.001). The emotional subscale scores of the MLwHFQ at baseline did not differ between survivors and non-survivors (6.9 (± 6.1) vs. 7.3 (± 6.1), p=0.380).

Table 1. Baseline characteristics according to mortality

	Total group (n=661)	Survivors (n=385)	Non-survivors (n=276)	p value*
Demographics				
Age (years)	71 ± 11	68 ± 12	74 ± 10	<.001
Male	62%	58%	64%	.147
Living alone	40%	39%	42%	.336
Smoking	17%	18%	15%	.290
Clinical characteristics				
LVEF %	34 ± 14	34 ± 14	34 ± 14	.916
NYHA III-IV	51%	45%	59%	<.001
Systolic blood pressure (mm/Hg)	118 ± 21	120 ± 21	116 ± 20	.039
Diastolic blood pressure (mm/Hg)	69 ± 12	70 ± 12	66 ± 12	<.001
Heart rate (bpm)	75 ± 13	75 ± 14	74 ± 12	.409
BNP (pg/mL) median (IQR)	447 (202-869)	342 (161-725)	572 (300-1110)	<.001
Sodium (mEq/L)	139 ± 4.7	139 ± 4.6	138 ± 4.9	.186
eGFR (ml/min/1.73m^2)	57 ± 22	61 ± 22	50 ± 20	<.001
Hypertension	44%	44%	43%	.968
Ischemic heart failure	42%	38%	46%	.041
Duration of heart failure (years)	2.7 ± 4.5	2.0 ± 3.8	3.7 ± 5.1	<.001
>1 previous heart failure hospitalization	33%	26%	43%	<.001
Medication				
ACE inhibitors/ARB	84%	87%	81%	.030
Beta-blockers	65%	68%	61%	.043
Diuretics	97%	96%	98%	.121

Table 1. (Continued) Baseline characteristics according to mortality

	Total group (n=661)	Survivors (n=385)	Non-survivors (n=276)	p value*
Comorbidities				
COPD	27%	25%	29%	.180
Diabetes	28%	23%	34%	.001
Stroke	9%	7%	12%	.029
Renal disease	7%	7%	8%	.444

* Comparison between survivors and non-survivors

Abbreviations: LVEF=left ventricular ejection fraction; NYHA=New York Heart Association functional class; BNP=B-type Natriuretic peptide; IQR=Inter Quartile Range; eGFR=estimated Glomerular Filtration Rate; ACE=Angiotensin Converting Enzyme; ARB=Angiotensin Receptor Blocker; COPD=Chronic Obstructive Pulmonary Disease

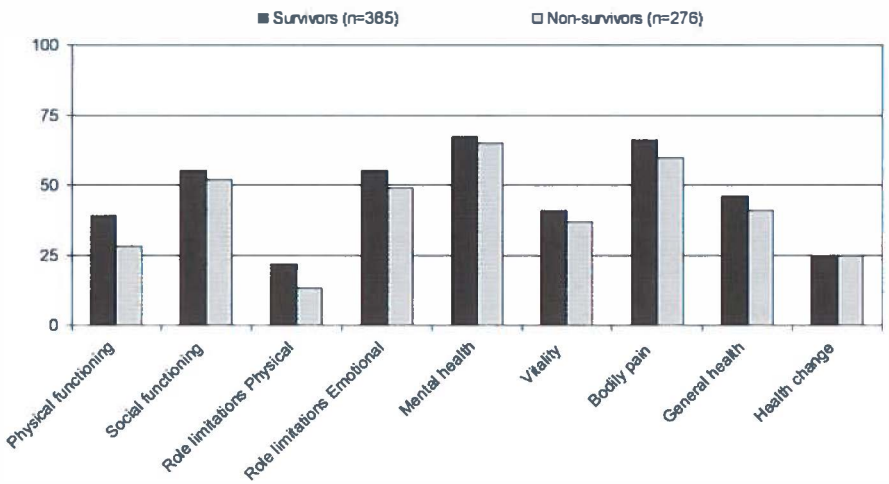


Figure 1. Quality of life as measured by the RAND36 at baseline according to mortality.

3.3 Survival analyses

Univariate analyses (model 1) show a HR of 1.15 (95% confidence interval 1.09-1.21) per 10 units on the physical functioning dimension of the RAND36, which indicates an increase of 15% in mortality per 10 units decrease on the physical functioning score. Furthermore a decrease in scores per 10 units on the role limitations physical, bodily pain, and general health dimensions of the RAND36 showed a significant increase in mortality (respectively 8%, 4%, and 12%, respectively). An increase in score per 10 units on the total score of the MLwHFQ and per one unit on the physical functioning score of the MLwHFQ also showed a significant increase of 7% and 2% in mortality (Table 2).

After adjusting the model for age, gender, NYHA, smoking, systolic blood pressure, diastolic blood pressure, heart rate, BNP-level, sodium-level, eGFR, ischaemic HF, duration of disease, previously hospitalized for HF more than once, ACE inhibitors/ARBs, beta-blockers, diuretics, diabetes, stroke and renal disease (model 3), the physical functioning and general health dimensions of the RAND36 were associated with mortality (Table 2).

Table 2. Cox proportional hazards regression of the quality of life subscales on time to mortality (n=661)

	Model 1		Model 2		Model 3	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Ladder of Life						
Well-being	1.04 (0.98-1.11)	.222	1.05 (0.98-1.12)	.148	1.01 (0.94-1.08)	.738
RAND-36 (per 10 units)						
Physical functioning	1.15 (1.09-1.21)	<.001	1.13 (1.07-1.20)	<.001	1.08 (1.02-1.14)	.008
Social functioning	1.01 (0.97-1.05)	.576	1.02 (0.99-1.06)	.343	0.98 (0.95-1.02)	.438
Role limitations Physical	1.08 (1.03-1.13)	.001	1.08 (1.04-1.13)	<.001	1.04 (0.99-1.08)	.128
Role limitations Emotional	1.02 (1.00-1.05)	.055	1.02 (1.00-1.05)	.071	1.01 (0.98-1.04)	.559
Mental Health	1.03 (0.98-1.08)	.289	1.06 (1.00-1.11)	.032	1.04 (0.99-1.10)	.150
Vitality	1.05 (1.00-1.11)	.053	1.07 (1.02-1.13)	.007	1.03 (0.98-1.09)	.256
Bodily Pain	1.04 (1.00-1.08)	.029	1.04 (1.00-1.07)	.044	1.03 (0.99-1.07)	.109
General Health	1.12 (1.05-1.20)	.001	1.13 (1.06-1.21)	<.001	1.08 (1.01-1.16)	.032
Health Change	1.01 (0.96-1.06)	.681	1.02 (0.96-1.07)	.557	1.00 (0.95-1.05)	.923
Minnesota Living with Heart Failure questionnaire						
Total (per 10 units)	1.07 (1.02-1.13)	.012	1.12 (1.06-1.19)	<.001	1.05 (0.98-1.12)	.172
Physical functioning	1.02 (1.01-1.03)	.002	1.02 (1.01-1.03)	<.001	1.01 (0.99-1.02)	.350
Emotional functioning	1.01 (0.99-1.03)	.302	1.03 (1.01-1.05)	.012	1.01 (0.99-1.03)	.304

Model 1: no adjustments

Model 2: adjustment for age and gender

Model 3: adjustment for age, gender, smoking, NYHA, systolic blood pressure, diastolic blood pressure, heart rate, BNP-level, sodium-level, eGFR, ischemic heart failure, duration of disease, previously hospitalized for heart failure >1, ACE-inhibitors/ARB, beta-blockers, diuretics, diabetes, stroke and renal disease

3.4 Patient characteristics related to low physical functioning and general health

Patient characteristics were compared between patients who scored in the lowest quartile of physical functioning (range 0-15) and general health (range 0-30) and the highest quartile (ranges respectively 50-100 and 55-100, respectively). Patients with a low QoL on physical functioning were older, more often female, more often in NYHA III-IV, had higher BNP levels at discharge, lower sodium levels, lower diastolic blood pressure, lower eGFRs, were more often diagnosed with chronic obstructive pulmonary disease (COPD), diabetes and stroke, had a longer duration of HF, were more often previously hospitalized for HF, and less often had a prescription of beta-blockers at discharge, than patients with high physical functioning (Table 3).

Patients with a low QoL on the general health dimension were also more often in NYHA III-IV, diagnosed with COPD and stroke, had suffered longer from HF, more often previously hospitalized for HF, had lower eGFRs, and were more often diagnosed with renal disease than patients with a high QoL on the general health dimension (Table 3).

During the 3-year follow-up period, 84 of the 157 patients (54%) with a low physical functioning score, and 39 of the 151 patients (26%) with a high physical functioning score, died ($p<0.001$) (Figure 2). Of the 133 patients with a low general health score, 75 patients (56%) died, compared to 54 of the 153 patients (35%) with a high general health score ($p<0.001$) (Figure 3).

Table 3. Patient characteristics; low versus high quality of life

	Low physical functioning (n=157)	High physical functioning (n=151)	p-value	Low general health (n=133)	High general health (n=153)	p-value
Demographics						
Age (years)	74 ± 10	67 ± 11	<.001	70 ± 12	72 ± 11	.301
Male	47%	72%	<.001	56%	59%	.678
Living alone	46%	36%	.079	39%	46%	.256
Smoking	16%	19%	.433	12%	18%	.177
Clinical characteristics						
LVEF %	34 ± 15	32 ± 14	.219	35 ± 15	35 ± 15	.975
NYHA III-IV	69%	26%	<.001	66%	33%	<.001
Systolic blood pressure (mm/Hg)	117 ± 22	121 ± 21	.109	115 ± 21	120 ± 21	.055
Diastolic blood pressure (mm/Hg)	67 ± 13	71 ± 12	.007	68 ± 13	70 ± 12	.103
Heart rate (bpm)	75 ± 13	74 ± 14	.474	74 ± 14	73 ± 13	.536
BNP (pg/mL) median (IQR)	497 (244-1090)	348 (162-747)	.017	502 (232-1070)	389 (179-801)	.125
Sodium (mEq/L)	137 ± 5.9	139 ± 4.3	<.001	138 ± 5.3	139 ± 5.2	.087
eGFR (ml/min/1.73m2)	51 ± 19	62 ± 21	<.001	52 ± 22	58 ± 19	.021
Hypertension	47%	42%	.399	44%	39%	.452
Ischemic heart failure	39%	40%	.874	39%	42%	.561

Table 3. (Continued) Patient characteristics; low versus high quality of life

	Low physical functioning (n=157)	High physical functioning (n=151)	p-value	Low general health (n=133)	High general health (n=153)	p-value
Duration of heart failure (years)	3.6 ± 5.1	1.4 ± 2.8	<.001	3.8 ± 5.5	1.6 ± 3.6	<.001
>1 previous heart failure hospitalization	47%	24%	<.001	47%	22%	<.001
Medication						
ACE inhibitors/ARB	82%	89%	.076	84%	86%	.739
Beta-blockers	58%	73%	.006	64%	67%	.625
Diuretics	97%	95%	.511	97%	97%	.900
Comorbidities						
COPD	33%	14%	<.001	35%	12%	<.001
Diabetes	39%	21%	<.001	25%	20%	.290
Stroke	13%	5%	.023	16%	4%	.001
Renal disease	7%	6%	.710	11%	3%	.008
Quality of life						
Physical functioning	6 ± 4	74 ± 15	<.001	21 ± 19	50 ± 29	<.001
General health	36 ± 17	55 ± 18	<.001	19 ± 7	70 ± 9	<.001

Abbreviations: LVEF=left ventricular ejection fraction; NYHA=New York Heart Association functional class; BNP=B-type Natriuretic peptide; IQR=Inter Quartile Range; eGFR=estimated Glomerular Filtration Rate; ACE=Angiotensin Converting Enzyme; ARB=Angiotensin Receptor Blocker; COPD=Chronic Obstructive Pulmonary Disease

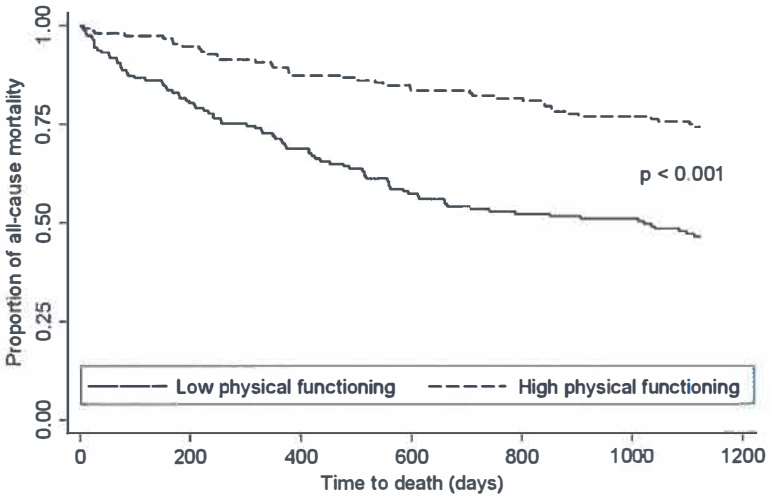


Figure 2. Kaplan-Meier curves for time to death in patients with low physical functioning and high physical functioning.

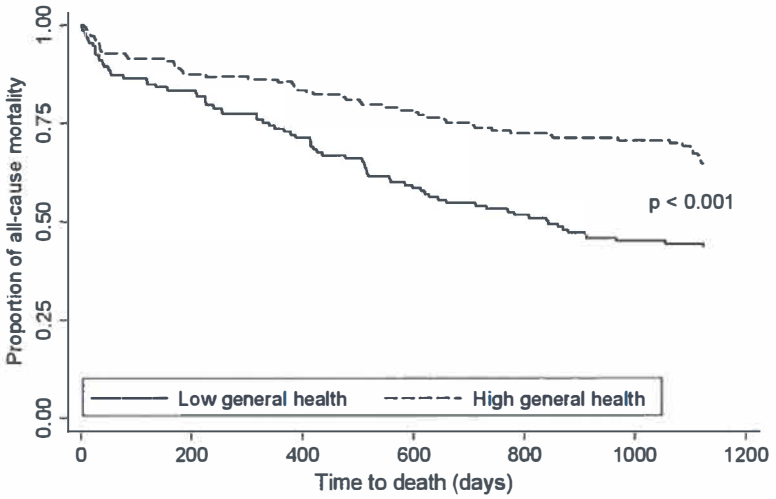


Figure 3. Kaplan-Meier curves for time to death in patients with low general health and high general health.

4. Discussion

The main finding of the present study is that QoL independently of BNP values predicts 3-year mortality in patients with HF. To our knowledge this is the first study in a large and clinically relevant group of HF patients in which the effect of QoL on mortality is adjusted for BNP levels, a widely accepted marker for disease severity and a prognostic tool to predict mortality.[11,22]

Previous research showed inconsistent results on physical QoL to be a predictor of mortality.[3] When looking at the four studies which used a disease-specific QoL questionnaire and had a follow-up period >2 years, all studies found a significant association between the physical component of their questionnaire and mortality.[6,7,23,24] However, our results on the physical dimension of the MLwHFQ being a predictor for survival independent of BNP levels do not confirm these findings. Studies including the physical dimensions of disease-generic QoL questionnaires to predict mortality, are not consistent.[6,7,25,26] Two studies did find physical functioning to be independently associated with mortality[7,25] and two other studies did not find this association.[6,24] However, these two studies had limitations in the generalizability of their results due to their relatively small sample size[26] and a very specific HF patient sample, namely male veterans.[6] Both studies which showed consistent findings had a relatively large (n=3375 and n=433) and a more generalizable HF patient sample.[7,25]

In our study we extend previous studies by taking the research to the next level by exploring which patients report low QoL in order to address future interventions for improving QoL, and reducing mortality. In our data we found several factors related to low QoL that could be used in identifying patients with low QoL, eg, higher age, female gender, being diagnosed with HF for longer, and co-morbidities. Other factors related to low QoL, which can be used to identify patients, but which also can be influenced by interventions and therefore possibly improve QoL, are high NYHA functional class (III-IV), low eGFRs and no prescription of beta-blockers.

To improve NYHA functional class, it can be suggested to include an exercise component in the treatment programmes of HF patients. Several studies have

shown that exercise programmes improve QoL.[27] Two meta-analyses of exercise-based rehabilitation clinical trials in patients with HF identified a significant benefit of exercise training on all-cause mortality and total cardiac mortality.[28,29] Furthermore, our results show that patients with a low QoL had fewer beta-blocker prescriptions. The effectiveness of beta-blockers for mortality is well tested,[1] and showed a trend towards improvement of QoL in patients receiving beta-blocker therapy.[30]

The current study underlines the importance of QoL in patients with HF.[31] Previous research on patients' preferences show that patients give equal or more importance to QoL when compared with length, and about half of a HF patient population is willing to select therapies that improve their QoL, even if this leads to shortening of life,[32,33] although one study showed the opposite results.[34] In the past study outcomes focused mainly on reducing hospitalizations and mortality. Nowadays, QoL is increasingly incorporated as an outcome measure in clinical trials.[35-37] Furthermore, in the HF guidelines, improving QoL is recognized as one of the major treatment goals.[15] Adding our findings that QoL is independently associated with mortality, to the relevance of QoL for individual patients, for research outcomes and for clinical practice, the value of QoL cannot be ignored. It is of great importance to develop and evaluate treatment programmes that effectively improve QoL in HF patients. However, there are few randomized studies that specifically focus on improving QoL in patients with HF. Some studies on disease management programmes have shown improvement in QoL as a result; unfortunately, the findings are inconsistent.[38]

It might be debated that the concepts QoL and depression are overlapping. Quality of life is defined by the World Health Organization as 'an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns'.[39] Depression is defined by the DSM-IV (Diagnostic and Statistic Manual of Mental Disorders, Fourth Edition) as a mental disorder that presents with depressed mood, loss of interest or pleasure, weight loss, feelings of guilt or low self-worth, disturbed sleep or appetite, fatigue and poor concentration, and

can be classified under the heading of the psychological function of the QoL domains.[40] From our COACH database, we previously published data that showed that 39% of patients with HF had depressive symptoms (Center for Epidemiological Studies Depression scale (CES-D) score >16) and having severe depressive symptoms was significantly associated with death and readmission within 18 months of follow-up after a hospital admission.[41] In the current study we did not include depressive symptoms measured by the CES-D, but did include several mental health and emotional dimensions of the different QoL questionnaires. These dimensions include fewer items than the CES-D, and are not specifically focused on depression, but more on emotions and mental health in general.

The present study is limited, in that the follow-up period for mortality was 3 years which is relatively short compared with other studies on QoL being a predictor for long-term mortality which have used follow-up periods of 5-7 years.[6,7] However, our sample size was relatively large (n=661) compared with the previous studies on long-term mortality, which had sample sizes of respectively 416 and 459 HF patients, respectively. Furthermore, our mortality rate was 42% and which is comparable with the mortality rates of both the other long-term follow-up studies (eg, 44% and 70%) and therefore high enough for reliable analyses on comparing QoL between survivors and non-survivors. A second limitation is generalizability of the study cohort. Only hospitalized patients with HF were included, which is only part of the total HF patient population.

In conclusion, the present study is the first study on QoL and long-term mortality in HF in which BNP levels were used as an objective marker to reflect the severity of HF. Our results show that QoL assessed during a hospitalization for HF is a predictor for 3-year mortality independent of BNP levels and a wide range of demographical and clinical variables. In particular general health and physical functioning assessed with a disease-generic QoL questionnaire provide prognostic information on survival in addition to other prognostic variables. Patients with low scores on these dimensions were more likely to be in NYHA III-IV, diagnosed

with comorbidities, suffered from HF for longer, had lower eGFRs, and had fewer beta-blocker prescriptions.

References

1. van Veldhuisen DJ, Cohen-Solal A, Böhm M, et al. Beta-blockade with nebivolol in elderly heart failure patients with impaired and preserved left ventricular ejection fraction. *J Am Coll Cardiol* 2009;**53**:2150-2158.
2. Hoekstra T, Lesman-Leegte I, van Veldhuisen DJ, Sanderman R, Jaarsma T. Quality of life is impaired similarly in heart failure patients with preserved and reduced ejaction fraction. *Eur J Heart Fail* 2011;**13**:1013-1018.
3. Mommersteeg PM, Denollet J, Spertus JA, Pedersen SS. Health status as a risk factor in cardiovascular disease: a systematic review of current evidence. *Am Heart J* 2009;**15**:208-218.
4. Schwarz KA, Elman CS. Identification of factors predictive of hospital readmissions for patients with heart failure. *Heart Lung* 2003;**32**:88-99.
5. Havranek EP, Lapuerta P, Simon TA, L'Italien G, Block AJ, Rouleau JL. A health perception score predicts cardiac events in patients with heart failure: results from the IMPRESS trial. *J Card Fail* 2001;**7**:153-157.
6. Subramanian U, Eckert G, Yeung A, Tierney WH. A single health status question had important prognostic value among outpatients with chronic heart failure. *J Clin Epidemiol* 2007;**60**:803-811.
7. Zuluaga MC, Guallar-Castillón P, López-García E, et al. Generic and disease-specific quality of life as a predictor of long-term mortality in heart failure. *Eur J Heart Fail* 2010;**12**:1372-1378.
8. Ekman I, Chassany O, Komajda M, et al. Heart rate reduction with ivabradine and health related quality of life in patients with chronic heart failure: results from the SHIFT study. *Eur Heart J* 2011;**32**:2395-2404.
9. van den Broek SAJ, van Veldhuisen DJ, de Graeff PA, Landsman MLJ, Hillege HL, Lie KI. Comparison between New York Heart Association classification and peak oxygen consumption in the assessment of functional status and prognosis in patients with mild to moderate chronic congestive heart failure secondary to either ischemic or idiopathic dilated cardiomyopathy. *Am J Cardiol* 1992;**70**:359-363.

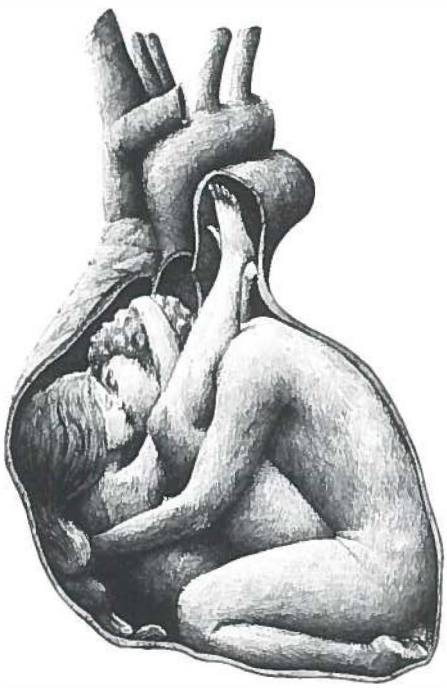
10. Raphael C, Briscoe C, Davies J, et al. Limitations of the New York Heart Association functional classification system and self-reported walking distances in chronic heart failure. *Heart* 2007;**93**:476-482.
11. Maisel A, Mueller C, Adams K Jr, et al. State of the art: using natriuretic peptide levels in clinical practice. *Eur J Heart Fail* 2008;**10**:824-839.
12. Jaarsma T, Van Der Wal MH, Hogenhuis J, et al. Design and methodology of the COACH study: a multicenter randomised Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure. *Eur J Heart Fail* 2004;**6**:227-233.
13. Jaarsma T, van der Wal MH, Lesman-Leegte I, et al. Effect of moderate or intensive disease management program on outcome in patients with heart failure: Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH). *Arch Intern Med* 2008;**168**:316-324.
14. Lesman-Leegte I, Jaarsma T, Coyne JC, Hillege HL, Van Veldhuisen DJ, Sanderman R. Quality of life and depressive symptoms in the elderly: a comparison between patients with heart failure and age- and gender-matched community controls. *J Card Fail* 2009;**15**:17-23.
15. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. *Eur J Heart Fail* 2008;**10**:933-989.
16. Hogenhuis J, Voors AA, Jaarsma T, Hillege HL, Hoes AW, van Veldhuisen DJ. Low prevalence of B-type natriuretic peptide levels <100 pg/mL in patients with heart failure at hospital discharge. *Am Heart J* 2006;**151**:1012e1-5.
17. Jenkins LS, Brodsky M, Schron E, et al. Quality of life in atrial fibrillation: the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Am Heart J* 2005;**149**:112-120.
18. Cantril H. *The pattern of human concerns*. New Brunswick, NJ: Rutgers University Press; 1965.

19. Van der Zee KI, Sanderman R, Heyink JW, de Haes H. Psychometric qualities of the RAND 36-item Health Survey 1.0: a multidimensional measure of general health status. *Int J Behav Med* 1996;**3**:104-122.
20. Ware JE. The SF-36 Health Survey. In: Spilker B, editor. *Quality of life and pharmacoeconomics in clinical trials.* Philadelphia, PA: Raven, 1996. p337-349.
21. Rector TS, Kubo SH, Cohn JN. Patients' self-assessment of their congestive heart failure: content, reliability and validity of a new measure, the Minnesota Living with Heart Failure questionnaire. *Heart Failure* 1987;**3**:198–209.
22. Faller H, Störk S, Schowalter M, et al. Is health-related quality of life an independent predictor of survival in patients with chronic heart failure? *J Psychosom Res* 2007;**63**:533-538.
23. Piotrowicz K, Noyes K, Lyness JM, et al. Physical functioning and mental well-being in association with health outcome in patients enrolled in the Multicenter Automatic Defibrillator Implantation Trial II. *Eur Heart J* 2007;**28**:601-607.
24. Murberg TA, Bru E, Svebak S, Tveteraås R, Aarsland T. Depressed mood and subjective health symptoms as predictors of mortality in patients with congestive heart failure: a two-years follow-up study. *Int J Psychiatry Med* 1999;**29**:311-326.
25. Konstam V, Salem D, Pouleur H, et al. Baseline quality of life as a predictor of mortality and hospitalization in 5,025 patients with congestive heart failure. SOLVD Investigations. Studies of Left Ventricular Dysfunction Investigators. *Am J Cardiol* 1996;**78**:890-895.
26. Mejhert M, Kahan T, Persson H, Edner M. Predicting readmissions and cardiovascular events in heart failure patients. *Int J Cardiol* 2006;**109**:108-113.
27. McKelvie RS. Exercise training in patients with heart failure: clinical outcome, safety and indications. *Heart Fail Rev* 2008;**13**:3-11.
28. Smart N, Marwick TH. Exercise training for patients with heart failure: a systematic review of factors that improve mortality and morbidity. *Am J Med* 2004;**116**:693-706.

29. Piepoli MF, Davos C, Francis DP, Coats AJS. Exercise training meta-analysis of trials in patients with chronic heart failure (ExTraMATCH). *BMJ* 2004;**328**:189-191.
30. Dobre D, van Jaarsveld CH, deJongste MJ, Haaijer Ruskamp FM, Ranchor AV. The effect of beta-blocker therapy on quality of life in heart failure patients: a systematic review and meta-analysis. *Pharmacoepidemiol Drug Saf* 2007;**16**:152-159.
31. Jaarsma T, Lesman-Leegte I. The value of the quality of life. *Eur J Heart Fail* 2010;**12**:901-902.
32. Lewis EF, Johnson PA, Johnson W, Collins C, Griffin L, Stevenson LW. Preferences for quality of life or survival expressed by patients with heart failure. *J Heart Lung Transplant* 2001;**20**:1016-1024.
33. Rector TS. Tschumperlin LK, Kubo SH, et al. Use of the living with heart failure questionnaire to ascertain patients' perspectives on improvement in quality of life versus risk of drug-induced death. *J Card Fail* 1995;**1**:201-206.
34. Brunner-La Rocca HP, Rickenbacher P, Muzzarelli S, et al. End-of-life preferences of elderly patients with chronic heart failure. *Eur Heart J* 2012;**33**:752-759.
35. de Vries AE, de Jong RM, van der Wal MH, Jaarsma T, van Dijk RB, Hillege HL. The value of INnovative ICT guided disease management combined with Telemonitoring in OUtpatient clinics for Chroning Heart failure patients. Design and methodology of the IN TOUCH study: a multicenter radomised trial. *BMC Health Serv Res* 2011;**11**:167.
36. Altenberger J, Parissis JT, Ulmer H, Poelzl; LevoRep Investigaters. Rationale and design of the multicentre randomized trial investigating the efficacy and safety of pulsed infusions of levosimendan in outpatients with advanced heart failure (LevoRep study). *Eur J Heart Fail* 2010;**12**:186-192.
37. Ghali JK, Tam SW, Ferdinand KC, et al. Effects of ACE inhibitors or beta-blockers in patients treated with the fixed-dose combination of isosorbide dinitrate/hydralazine in the African-American Heart Failure Trial. *Am J Cardiovasc Drugs* 2007;**7**:373-380.

38. Jaarsma T, Johansson P, Agren S, Strömberg A. Quality of life and symptoms of depression in advanced heart failure patients and their partners. *Curr Opin Support Palliat Care* 201;**4**:233-237.
39. Kuyken W, on behalf of the WHOQOL Group. The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. *Soc Sci Med* 1995;**41**:1403-1409.
40. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders Fourth Edition.* Text revision. Washington DC: American Psychiatric Association; 2000.
41. Lesman-Leegte I, van Veldhuisen DJ, Hillege HL, Moser D, Sanderman R, Jaarsma T. Depressive symptoms and outcomes in patients with heart failure: data from the COACH study. *Eur J Heart Fail* 2009;**11**:1202-1207.

Chapter 3:
Quality of life is impaired similarly in heart failure patients with preserved and reduced ejection fraction



Tialda Hoekstra, Ivonne Lesman-Leegte, Dirk J. van Veldhuisen, Robbert Sanderman, Tiny Jaarsma

European Journal of Heart Failure 2011;13:1013-1018

Abstract

Aims: To compare quality of life (QoL) in heart failure(HF) patients with preserved ejection fraction (HF-PEF) and HF patients with reduced ejection fraction (HF-REF) in a well-defined HF population.

Methods and results: Patients with HF-PEF (left ventricular ejection fraction (LVEF) ≥40%) were matched by age and gender to patients with HF-REF (LVEF <40%). In the current study, we only included HF patients with a B-type natriuretic peptide level (BNP) >100 pg/mL. Quality of life was assessed by Cantril's Ladder of Life, RAND-36 and the Minnesota Living with Heart Failure questionnaire, and impairment of QoL was adjusted for by BNP as a marker for severity of HF.

We examined a total of 290 HF patients, of whom 145 had HF-PEF (41% female; age 72 ± 10; LVEF 51 ± 8%) and 145 had HF-REF (41% female; age 73 ± 10, LVEF 26 ± 7%). All HF patients reported markedly low scores of QoL, both on the general and disease specific QoL questionnaires. Quality of life between patients with HF-PEF and HF-REF did not differ significantly. When adjusting the QoL scores for BNP, an association between QoL and LVEF was not found, i.e. patients with HF-PEF and HF-REF with similar BNP levels, had the same impairment in QoL.

Conclusion: Quality of life is similarly impaired in patients with HF-PEF as in HF-REF. These findings further support the need for more pharmacological and non-pharmacological studies in patients with HF-PEF.

1. Introduction

Heart failure (HF) has a major impact on the quality of life (QoL) of patients, in physical, mental and social domains.[1,2] Patients with HF have a significantly lower QoL than an age- and gender-matched members of the community.[3] But even compared to other chronically ill patients, patients with HF have similar or even more impaired physical and mental health.[4] In recent years, patient-centred outcomes, such as QoL, have gained greater importance, particularly because life expectancies for HF patients have increased, and HF patients have to adjust to living with a chronic condition and for many (elderly) patients QoL appears to be more important than longer survival.[5,6] In addition, impaired QoL is increasingly associated with a poor outcome in HF.[7,8]

In HF patients, the large majority of studies have been conducted in patients with a reduced ejection fraction (HF-REF). However, at least 50% of all HF patients have HF with a preserved ejection fraction (HF-PEF).[9,10] Symptoms and signs often seem similar in patients with HF-PEF and HF-REF.[11] However, no treatment has been shown to be effective in HF-PEF patients, and current guidelines do not support the use of any class of drugs in this patient category.[1] There is only limited knowledge about the QoL of patients with HF-PEF compared with patients with HF-REF. Five studies that compared QoL in these two populations showed inconsistent results, reporting either no significant differences in QoL[11-14] or more impaired QoL in patients with HF-REF.[15]

Previous reports about the QoL of patients with HF-PEF were not only relatively small, but they also used the New York Heart Association (NYHA) functional class to adjust for severity of HF, which of course affects QoL as well. Indeed, none of the aforementioned studies used an objective diagnostic marker for the severity (and presence) of HF. Especially in patients with HF-PEF, the diagnosis of HF is often more difficult, and in fact some patients with assumed HF-PEF do not have HF but suffer from another condition such as anaemia, lung disease, or even depression.[9,10]

We therefore studied a large number of QoL measurements in a group of patients with HF-PEF, compared to a matched group of patients with HF-REF. In order

to try to obtain an objective parameter for the severity of HF, we used plasma levels of B-type natriuretic peptide (BNP), since this is an independent and reliable marker of HF severity.[16]

2. Methods

2.1 Patient population

Data from patients participating in the COACH (Coordinating study evaluating Advising and Counselling in Heart failure) study were used. COACH was a multicenter, randomized clinical trial on the effect of a disease management programme in HF, the design and main results have been published.[17,18] In short, 1023 patients from 17 hospitals in The Netherlands were enrolled in the COACH study. Patients were included in the study at the end of hospitalization for HF (NYHA functional class II to IV), with HF as the primary diagnosis. The diagnosis was based on a combination of typical signs and symptoms according to the European Society of Cardiology guidelines[1] for which a hospital stay was considered necessary, and the need for intravenously administered medication. During hospitalization all patients received standard care, both pharmacological and non-pharmacological, according to the guidelines[1] in a cardiology ward, staffed by cardiologists and registered nurses. Patients were 18 years or older and had evidence of structural underlying heart disease as shown at cardiovascular imaging. Exclusion criteria were: concurrent inclusion in a study requiring additional visits to research health care personnel; restrictions that made the patient unable to fill in data collection forms; invasive intervention within the last 6 months or planned during the following 3 months; or ongoing evaluation for heart transplantation. All patients gave written informed consent. Although all patients in the COACH study had HF as the primary diagnosis and were included in experienced HF centres, in the current analyses we only included patients who had a BNP plasma level > 100 pg/mL, to strengthen the evidence for a diagnosis of HF in all patients.[1,19]

The study was performed in accordance with the principles outlined in the Declaration of Helsinki and was approved by the Medical Ethics Committee in each participating centre.

2.2 Data collection

2.2.1 Left ventricular ejection fraction and brain natriuretic peptide

Data on left ventricular function (LV function) were obtained by standard trans-thoracic echocardiography. These data were used to distinguish between HF-PEF and HF-REF. Reduced LV systolic function was defined as an LVEF <40% (HF-REF); and preserved LV systolic function was defined as an LVEF ≥40% (HF-PEF). In the current analyses, only patients with complete echocardiographic data were included. Plasma BNP levels were determined within 4h of blood collection (1mL blood, collected in EDTA), on the day of hospital discharge or on the day before hospital discharge. All BNP measurements were performed using a fluorescence immunoassay kit (Triage®; Biosite Incorporated, San Diego, CA, USA).[19]

2.2.2 Quality of life

Data on QoL in the COACH study were collected during the index hospitalization and during follow-up. To minimise the confounding effect of the recent hospitalization on QoL, we used QoL data collected one month after discharge. Quality of life was assessed in three different ways: global well-being, general QoL and disease specific QoL.

Global well-being was assessed by Cantril's Ladder of Life. This is a single-item measure which asks the patient to rate their sense of well being on a ladder, with 10 reflecting the best possible life imaginable and 0 reflecting the worst possible life imaginable. A higher score indicates better well being.[20]

General QoL was assessed by the Medical Outcome Study 36-item General Health Survey (RAND-36), a self-report questionnaire of general health status. It is a well-validated generic, 36-item questionnaire that includes 9 health concepts that represent dimensions of QoL: physical functioning, social functioning, role

limitations because of physical functioning, role limitations because of emotional functioning, mental health, vitality, bodily pain, general health and perceived health change. Each dimension has a score between 0 and 100; a higher score means better health.[21]

Disease specific QoL was measured with the Minnesota Living with Heart Failure (MLwHF) questionnaire.[22] The MLwHF questionnaire is a 21-item questionnaire assessing how HF has affected the life of the respondent during the last month. The MLwHF has a scoring range of zero for no impairment as a result of HF to 105 for maximum impairment. The questions cover symptoms and signs relevant to HF, physical activity, social interaction, sexual activity, work and emotions. Three scores can be determined: an overall score (21 items, 0-105), the physical dimension (8 items, 0-40) and the emotional dimension (5 items, 0-25). Higher MLwHF scores mean a worse QoL.

2.3 Statistical analysis

The two patient groups (HF-PEF and HF-REF) were matched by age (10 year categories) and gender to have a fair test of differences.[23] First, descriptive statistics were used to characterize the HF-PEF and HF-REF patients. For continuous variables means and standard deviations and for categorical variables frequencies with percentages were used. Secondly, differences on QoL between both HF patient groups were univariately tested using the Mann-Whitney U test. Thirdly, a Spearman correlation was calculated between BNP and QoL in the total group to analyze the relation between QoL and BNP levels. Finally, to adjust for an objective measure of the severity of HF, an Analysis of Covariance (ANCOVA) was performed using QoL scores as the dependent variable and BNP as the covariate. The more subjective measure for the severity of HF, NYHA functional class, was not included in the analysis because of an overlap with (physical dimensions of) QoL.

Analyses were performed using SPSS for windows version 16 (SPSS Inc., Chicago, USA). Outcomes were considered statistically significant when $p<0.05$.

3. Results

3.1 Patients

Of the 1023 patients included in the main COACH study, an LVEF measurement and a BNP level was available in 698 patients. Of these, 627 patients had a BNP level >100 pg/mL. Within this patient sample, QoL questionnaires at one month after discharge were completed by 485 patients. Only patients who completed all questionnaires were included in the current study. Of these, 31% had an LVEF ≥40% and 69% had an LVEF <40%.

After matching for age and gender, both patient groups consisted of 145 patients. Due to the process of matching, 195 HF patients (190 LVEF <40%, 5 LVEF ≥40%) were not analyzed. These excluded HF patients were younger, more often male, had a lower mean LVEF, and their QoL was slightly better on physical functioning of the MLwHF questionnaire. ($p<0.05$). All other domains of QoL, and the BNP levels were similar in both groups.

3.2 Characteristics

Patients with HF-PEF were on average 72 (± 10) years old, 41% were female and the mean LVEF was 50% (± 8%). Patients with HF-REF were on average 72 (± 10) years old, 41% were female and the mean LVEF was 26% (± 7%) (Table 1). In patients with HF-PEF the prevalence of hypertension was higher than in patients with HF-REF ($p=0.025$). Brain natriuretic peptide levels were significantly higher in the HF-REF patient group ($p=0.001$). More patients with HF-REF were classified as NYHA functional class III-IV at discharge than patients with HF-PEF ($p<0.001$) (Table 1).

Table 1: Demographic and clinical characteristics of the matched patient groups at discharge

	HF-REF (n=145)	HF-PEF (n=145)	p-value
Demographics			
Age (years)	72 ± 10	72 ± 10	.739
Female	41%	41%	1.000
Clinical characteristics			
LVEF %	26 ± 7	50 ± 8	<.001
NYHA III-IV	61%	38%	<.001
BNP (pg/mL) median (IQR)	516 (290-1125)	370 (215-755)	.001
Hypertension	37%	50%	.025
Ischaemic heart failure	43%	43%	.946
Myocardial infarction	46%	37%	.095
Duration of heart failure (years)	2.7 ± 4.3	2.7 ± 4.5	.853
Medication			
ACE-inhibitors/ARB	88%	81%	.102
Beta-blockers	67%	66%	.901
Diuretics	97%	97%	1.000
Comorbidities			
COPD	22%	30%	.109
Diabetes	30%	28%	.699
Stroke	10%	7%	.394

Abbreviations: LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; BNP=B-type Natriuretic peptide; IQR=Inter Quartile Range; ACE=Angiotensin Converting Enzyme; ARB=Angiotensin Receptor Blocker; COPD=Chronic Obstructive Pulmonary Disease

3.3 Quality of Life

Global wellbeing, as measured with Cantril's Ladder of Life, did not differ significantly between patients with HF-PEF and HF-REF (6.3 vs. 6.3, p=0.862).
Scores of all dimensions of the RAND-36 varied between 17 and 78, on the theoretical range between 0-100, with the lowest scores for role limitations physical, physical functioning and health change. None of the dimensions of the general QoL, measured with RAND-36, differ significantly between HP-REF and HF-REF patients, except for bodily pain (HF-PEF vs. HF-REF, 70 vs. 78, p=0.006).
The mean score on the total scale of the MLwHF questionnaire was 41. On the physical and emotional subscales, mean scores were 21 and 8, respectively. Also on the MLwHF questionnaire, patients with HF-PEF did not rate their QoL different than patients with HF-REF. The total scores as well as the scores on the physical and emotional functioning subscales did not differ significantly between both groups (Table 2).

3.4 Relationship between brain natriuretic peptide and quality of life

Global wellbeing was not significantly related to BNP levels in the total patient group (n=290). Of the dimensions of the RAND-36, health change was significantly correlated to BNP levels (rho=.124, $p<0.05$). All other dimensions of the RAND-36 were not significantly correlated to BNP levels. Disease specific QoL, as measured with the MLwHF questionnaire, was significantly correlated with BNP levels. There was a correlation with the total score (rho=.132, $p<0.05$) and the physical subscale of the MLwHF questionnaire (rho=.151, $p<0.01$). There was no significant correlation between BNP levels and the emotional subscale of the MLwHF questionnaire.

Table 2. Quality of life in heart failure patients with reduced (HF-REF) and preserved left ventricular ejection fraction (HF-PEF)

	Total (n=290)		HF-REF (n=145)		HF-PEF (n=145)		p-value*
	Baseline	1 month	Baseline	1 month	Baseline	1 month	
Ladder of Life							
Well-being	6.3 ± 2	6.3 ± 2	6.5 ± 2	6.3 ± 2	6.2 ± 2	6.3 ± 1	.866
RAND-36							
Physical functioning	34 ± 27	40 ± 28	32 ± 27	38 ± 27	35 ± 27	43 ± 28	.165
Social functioning	53 ± 32	57 ± 29	51 ± 33	55 ± 31	55 ± 31	59 ± 27	.296
Role limitations Physical	18 ± 33	20 ± 34	19 ± 33	17 ± 33	17 ± 33	22 ± 35	.156
Role limitations Emotional	51 ± 45	48 ± 46	53 ± 46	48 ± 46	50 ± 46	49 ± 46	.807
Mental Health	67 ± 23	70 ± 21	67 ± 24	69 ± 21	66 ± 21	70 ± 20	.908
Vitality	41 ± 23	49 ± 23	42 ± 25	48 ± 23	39 ± 22	49 ± 23	.938
Bodily Pain	63 ± 33	74 ± 28	66 ± 32	78 ± 26	61 ± 33	70 ± 28	.006
General Health	44 ± 18	45 ± 19	44 ± 17	45 ± 19	44 ± 19	45 ± 19	.956
Health Change	26 ± 23	34 ± 29	25 ± 23	34 ± 29	27 ± 23	34 ± 29	.817
Minnesota Living with Heart Failure							
Total	45 ± 21	41 ± 22	46 ± 21	41 ± 23	44 ± 21	41 ± 21	.816
Physical functioning	24 ± 10	21 ± 11	25 ± 10	21 ± 11	24 ± 11	20 ± 11	.704
Emotional functioning	7 ± 6	8 ± 6	7 ± 6	8 ± 6	7 ± 6	8 ± 6	.692

* Comparison between HF-REF and HF-PEF patient groups at 1 month after discharge

3.5 Adjustment for brain natriuretic peptide

After adjusting the QoL scores for BNP level, QoL was not associated with LVEF. There were no differences in the adjusted global wellbeing scores between patients with HF-PEF and HF-REF (6.3 vs. 6.3, p=0.671) (Figure 1). The adjusted general QoL did not differ between the two groups, except for the bodily pain dimension, in which patients with HF-PEF had a significantly lower score, which means worse QoL (70 vs. 77, p=0.020) (Figure 1) compared with the HF-REF. The scores on the disease specific QoL questionnaire (MLwHF) did not differ on the total score or on both subscales (physical and emotional functioning) between the two groups (Figure 1).

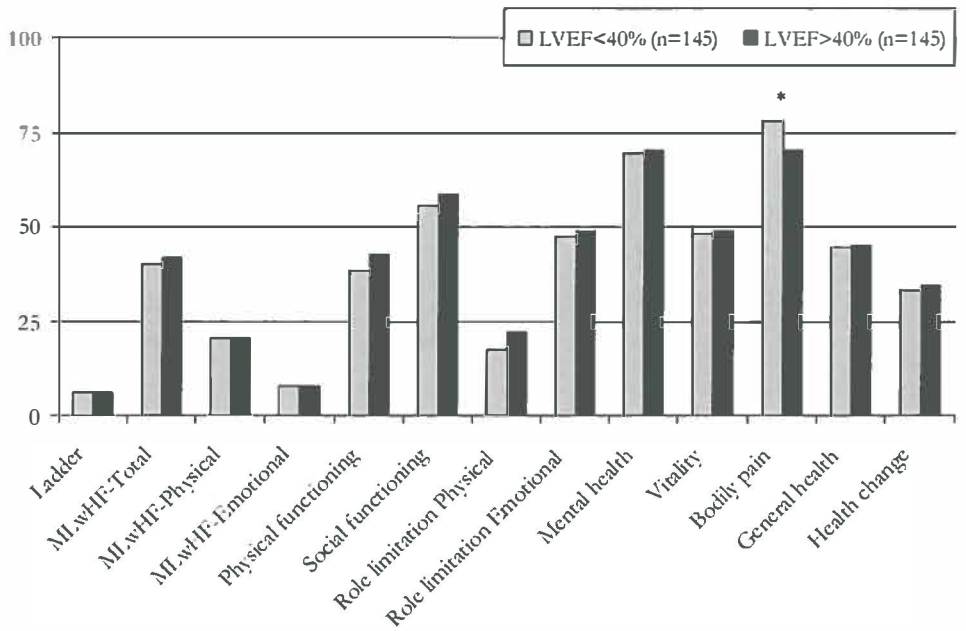


Figure 1. Quality of life in patients with HF-REF and HF-PEF, multivariate tested and adjusted for brain natriuretic peptide. * p<0.05.

4. Discussion

The main finding of the present study is that QoL in patients with HF-PEF is as severely affected as it is in patients with HF-REF. This similarity between HF-PEF and HF-REF patients is consistent on several domains of QoL, both disease generic and disease specific. When we adjusted the QoL scores for BNP, as a marker for the severity of the disease, an association between QoL and LVEF was not found, despite the significant correlation between BNP and several QoL domains (health change of the RAND-36, physical and total scores of the MLwHF questionnaire) i.e. patients with HF-PEF and HF-REF with similar BNP levels, had the same impairment in QoL.

Although the two patient groups differed significantly in terms of the number of patients in NYHA III-IV at discharge, and a linear association between NYHA and (physical) QoL could be suggested, we did not find significant differences in QoL scores. This might be due to the fact that QoL includes more dimensions than physical function alone as measured by NYHA functional class. Although NYHA functional class definitely influences QoL, eg, the scores between both groups differed the most for the physical function dimensions, the QoL scores between the two groups did not differ significantly.

It is well-known known that QoL is affected by gender and age and patients with HF-PEF and HF-REF are different regarding these two variables. Patients with HF-PEF are more often female and older[9,10] and in general it would seem that QoL is lower in patients with HF-PEF. By using the matching technique (on age and gender[23]) we showed, however, that possible differences in QoL are not due to differences in LVEF but probably caused by the presence of more patients with higher age and female sex in the HF-PEF group compared to the HF-REF group.

To our knowledge this is the first study to compare QoL between HF-PEF and HF-REF patients that has used an independent and reliable marker for the severity of HF (i.e. BNP). Although the diagnosis of HF in the COACH study was already well defined, in the current study we only included patients with plasma BNP levels >100 pg/mL. In previous studies, HF patients were defined using more subjective criteria such as NYHA class or an admission to the hospital with a

cardiovascular problem in the previous 6 months,[13] an admission to the cardiology ward with symptoms of HF,[11] the application of the European Study Group criteria[12] or a clinical score of three or greater from NHANES I (National Health and Nutrition Examination Survey I).[14,15] There are several possible subjective and objective markers of disease severity in HF, for example NYHA functional class, sodium restriction, and renal dysfunction. We chose to use BNP levels as a marker for disease severity in our analysis, because this is an objective and a generally accepted measure for the severity of HF,[1] and has no direct overlap with (physical dimensions of) QoL like NYHA functional class.

There are almost no studies published on the comparison of QoL between HF-PEF and HF-REF. One of the few studies that have been published is by Lewis et al.[13] from the large CHARM population (n=2709), who reported that QoL was associated with LVEF and was equally impaired in HF-PEF and HF-REF. Our results further extend the findings of this previous study in several respects. First, our study had the advantage of using an objective marker for the presence of HF (LVEF combined with elevated BNP levels in both the HF-PEF and HF-REF groups), making us more confident that the patients with HF-PEF had HF and were not suffering from different diagnoses. Secondly, our study extends previous observations by using multiple QoL assessments to demonstrate the similarity in different domains of QoL, such as general well being, physical and social functioning, role limitations and disease specific QoL between the two groups. Thirdly, we deliberately chose to match the two patient groups instead of putting age and gender into the multivariate model to have a fair test of comparison. In QoL research between groups of patients, statistical analyses often ignore the meaning of differences in age and gender. When age and gender are treated as nuisance variables and are dealt with by statistical control, we are actually forming a counterfactual situation. In this sense 'controlling for age and gender' substantively means attempting to eliminate the effects of significant differences in role responsibilities.[23] Quality of life is experienced differently by men and women, and by younger and older patients, therefore we decided to match the two patient groups instead of controlling for age.

While patients with HF-PEF appear to have similar symptoms of HF and their prognosis is as poor as those with HF-REF[9,10,24] no treatment option has been proven effective in this population. Although, favourable effects on clinical endpoints (hospitalizations and mortality) have been suggested in some (sub-) populations of patients with HF-PEF for angiotensin converting enzyme (ACE) inhibitors,[25] angiotensin receptor blockers,[26] and beta-blockers,[27] none of these agents has shown a significant benefit on outcome in large randomized studies, and none of them has therefore received a recommendation in current guidelines.[1] When it comes to QoL, few studies have focused specifically on the HF-PEF population. Nevertheless, it appears that QoL is gaining increasing attention in HF-PEF, and in one recently reported study with valsartan[28] and in another ongoing study with spironolactone,[29] QoL is one of the important endpoints.

There are a few limitations to the present study. First, due to the process of matching 195 patients, mostly patients with HF-REF, were excluded from the analysis. However, we deliberately chose to match the two patient groups instead of including age and gender in the multivariate analysis to have a fair test of comparison, and gain a more representative clinical insight in the comparison of QoL between patients with HF-PEF and HF-REF.[23] Secondly, we defined HF-PEF as an LVEF ≥40%. At present the cut-off point of LVEF to diagnose HF-REF or HF-PEF is still a matter of debate, we chose a cut-off of 40% because it has been used in other large databases,[13] and because otherwise very few patients would have been included in the HF-PEF group. Thirdly, in the current study we used QoL data at one month after discharge, while BNP levels were collected at discharge. We deliberately chose to use the QoL data at one month after discharge to minimise the confounding effect of the recent hospitalization.

In conclusion, patients with symptomatic HF with preserved LVEF (HF-PEF) and elevated levels of BNP suffer from their HF as much as age- and gender-matched HF patients with HF-REF, resulting in a comparably low QoL and well-being. Pharmacological and non-pharmacological management interventions that have proved to be successful in HF-REF patients to improve QoL, might be

successful in HF-PEF too. Further research to test whether these interventions can improve QoL is now needed.

References

1. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. *Eur J Heart Fail* 2008;**10**:933-989.
2. Lesman-Leegte I, van Veldhuisen DJ, Hillege HL, Moser D, Sanderman R, Jaarsma T. Depressive symptoms and outcomes in patients with heart failure: data from the COACH study. *Eur J Heart Fail* 2009;**11**:1202-1207.
3. Lesman-Leegte I, Jaarsma T, Coyne JC, Hillege HL, Van Veldhuisen DJ, Sanderman R. Quality of life and depressive symptoms in the elderly: a comparison between patients with heart failure and age- and gender-matched community controls. *J Card Fail* 2009;**15**:17-23.
4. Juenger J, Schellberg D, Kraemer S, et al. Health related quality of life in patients with congestive heart failure: comparison with other chronic diseases and relation to functional variables. *Heart* 2002;**87**:235-241.
5. Stevenson LW. Design of therapy for advanced hear failure. *Eur J Heart Fail* 2005;**7**:323-331.
6. Jaarsma T, Beattie JM, Ryder M, et al. Palliative care in heart failure: a position statement from the palliative care workshop of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2009;**11**:433-443.
7. Iqbal J, Francis L, Reid J, Murray S, Denvir M. Quality of life in patients with chronic heart failure and their carers: a 3-year follow-up study assessing hospitalization and mortality. *Eur J Heart Fail* 2010;**12**:1002-1008.
8. Zuluaga MC, Guallar-Castillón P, López-García E, et al. Generic and disease-specific quality of life as a predictor of long-term mortality in heart failure. *Eur J Heart Fail* 2010;**12**:1372-1378.
9. Paulus WJ, van Ballegoij JJ. Treatment of heart failure with normal ejection fraction: an inconvenient truth! *J Am Coll Cardiol* 2010;**55**:526-537.

10. Kindermann M, Reil JC, Pieske B, van Veldhuisen DJ, Böhm M. Heart failure with normal left ventricular ejection fraction: what is the evidence? *Trends Cardiovasc Med* 2008;**18**:280-292.
11. Jaarsma T, Halfens R, Abu-Saad HH, Dracup K, Stappers J, van Ree J. Quality of life in older patients with systolic and diastolic heart failure. *Eur J Heart Fail* 1999;**1**:151-60.
12. O'Mahony MS, Sim MF, Ho SF, Steward JA, Buchalter M, Burr M. Diastolic heart failure in older people. *Age Ageing* 2003;**32**:519-524.
13. Lewis EF, Lamas GA, O'Meara E, et al. Characterization of health-related quality of life in heart failure patients with preserved versus low ejection fraction in CHARM. *Eur J Heart Fail* 2007;**9**:83-91.
14. Austin BA, Wang Y, Smith GL, Vaccarine V, Krumholz HM, McNamara RL. Systolic function as a predictor of mortality and quality of life in long-term survivors with heart failure. *Clin Cardiol* 2008;**31**:119-124.
15. Kitzman DW, Little WC, Brubaker PH, et al. Pathophysiological characterization of isolated diastolic heart failure in comparison to systolic heart failure. *JAMA* 2002;**288**:2144-2150.
16. Maisel A, Mueller C, Adams K Jr, et al. State of the art: using natriuretic peptide levels in clinical practice. *Eur J Heart Fail* 2008;**10**:824-839.
17. Jaarsma T, Van Der Wal MH, Hogenhuis J, et al. Design and methodology of the COACH study: a multicenter randomised Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure. *Eur J Heart Fail* 2004;**6**:227-233.
18. Jaarsma T, van der Wal MH, Lesman-Leegte I, et al. Effect of moderate or intensive disease management program on outcome in patients with heart failure: Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH). *Arch Intern Med* 2008;**168**:316-324.
19. Hogenhuis J, Voors AA, Jaarsma T, Hillege HL, Hoes AW, van Veldhuisen DJ. Low prevalence of B-type natriuretic peptide levels <100 pg/mL in patients with heart failure at hospital discharge. *Am Heart J* 2006;**151**:1012e1-1012e5.

20. Cantril H. *The pattern of human concerns*. New Brunswick, NJ: Rutgers University Press; 1965.
21. Van der Zee KI, Sanderman R, Heyink JW, de Haes H. Psychometric qualities of the RAND 36-item Health Survey 1.0: a multidimensional measure of general health status. *Int J Behav Med* 1996;**3**:104-122.
22. Rector TS, Kubo SH, Cohn JN, Patients' self-assessment of their congestive heart failure: content, reliability and validity of a new measure, the Minnesota Living with Heart Failure questionnaire. *Heart Failure* 1987;**3**:198–209.
23. Sanderman R, Coyne JC, Ranchor AV. Age: nuisance variable to be eliminated with statistical control or important concern? *Patient Educ Couns* 2006;**61**:315-316.
24. Lenzen MJ, Scholte op Reimer WJ, Boersma E, et al. Differences between patients with a preserved and a depressed left ventricular function: a report from the EuroHeart Failure Survey. *Eur Heart J* 2004;**25**:1214-1220.
25. Cleland JG, Tendera M, Adamus J, Freemantle N, Plonski L, Taylor J. The perindopril in elderly people with chronic heart failure (PEP-CHF) study. *Eur Heart* J 2006;**27**:2338-2345.
26. Yusuf S, Pfeffer MA, Swedberg K, et al. Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: the CHARM-Preserved Trial. *Lancet* 2003;**362**:777-781.
27. van Veldhuisen DJ, Cohen-Solal A, Böhm M, et al. Beta-blockade with nebivolol in elderly heart failure patients with impaired and preserved left ventricular ejection fraction: Data from SENIORS (Study of Effects of Nebivolol Intervention on Outcomes and Rehospitalization in Seniors With Heart Failure). *J Am Coll Cardiol* 2009; **53**:2150-2158.
28. Parthasarathy HK, Pieske B, Weisskopf M, et al. A randomized, double-blind, placebo-controlled study to determine the effects of valsartan on exercise time in patients with symptomatic heart failure with preserved ejection fraction. *Eur J Heart Fail* 2009;**11**:980-989.

29. Edelmann F, Schmidt AG, Gelbrich G, et al Rationale and design of the 'aldosterone receptor blockade in diastolic heart failure' trial: a double-blind, randomized, placebo-controlled, parallel group study to determine the effects of spironolactone on exercise capacity and diastolic function in patients with symptomatic diastolic heart failure (Aldo-DHF). *Eur J Heart Fail* 2010;**12**:874-882.

Chapter 4:
Characteristics of heart failure patients with a preserved ejection fraction and low BNP-levels

Tialda Hoekstra, Tiny Jaarsma, Dirk J. van Veldhuisen, Robbert Sanderman, Ivonne Lesman-Leegte

Abstract

Aims: The diagnosis of heart failure with a preserved ejection fraction (HF-PEF) is often difficult. Natriuretic peptides such as B-type Natriuretic Peptide (BNP) may possibly be used in the diagnosis. Current guidelines use a cut-off level for BNP of >100pg/ml in order to confirm the diagnosis of HF. All patients included in the COACH study were assumed to have HF, based on HF symptoms. To examine whether HF-PEF patients with BNP-levels<100pg/ml differ from HF-PEF patients who have BNP-levels>100pg/ml, we compared clinical characteristics, HF symptoms and quality of life (QoL) measurements in a group of HF-PEF patients who were enrolled in COACH.

Methods: Thirty-seven patients with BNP-levels<100pg/ml and left ventricular ejection fraction (LVEF)≥40% (54% male, age 72 years) were compared with 162 patients with BNP-levels>100pg/ml and LVEF≥40% (57% male, age 73 years). Data on BNP-levels, QoL, demographic and clinical variables were assessed at discharge for a hospital admission for HF.

Results: Patients with low BNP-levels were more often in NYHA III-IV (60% vs. 38%, p=0.016), more often obese (47% vs. 24%, p=0.007), and had a higher mean LVEF (54% vs. 50%, p=0.003) than patients with high BNP-levels. Both patient groups did not differ on other comorbidities like anaemia, COPD, diabetes and hypertension. Quality of life between patients with low and high BNP-levels did not differ significantly, although there was a clinical relevant difference in QoL in which patients with low BNP-levels had worse physical functioning, general health and bodily pain. Of all the HF-symptoms, only loss of appetite differed significantly between both groups, and was less often reported by patients with high BNP-levels (33% vs. 52%, p=0.044).

Conclusion: Patients with a preserved ejection fraction and BNP-levels<100pg/ml do not differ on a broad range of characteristics, comorbidities, HF symptoms and QoL parameters from patients with BNP-levels>100pg/ml, except for obesity.

1. Introduction

There is an increasing interest in patients with heart failure with preserved ejection fraction (HF-PEF). The prevalence of HF-PEF among patients with heart failure (HF) is high; at least 50% of all HF patients have HF-PEF.[1,2] Symptoms and signs often seem similar in patients with HF-PEF and HF-REF, and quality of life (QoL) is equally impaired.[3,4] In general, patients with HF-PEF are older, more often female, more predominantly hypertensive, and have a higher prevalence of atrial fibrillation, but a lower prevalence of coronary artery disease compared to patients with heart failure and reduced ejection fraction (HF-REF).[5] Furthermore, the prevalence of comorbidities, like obesity, anaemia, chronic lung disease and diabetes mellitus, also appear to be highly prevalent in patients with HF-PEF.[5] Due to the presence of these comorbidities, including symptoms which resemble HF symptoms, the diagnosis of HF is often difficult, and in fact some patients with assumed HF-PEF do not have HF, but suffer from another condition such as anaemia, lung disease, or depression.[1,2]

Nowadays the guidelines of the European Society of Cardiology state that untreated patients with symptoms of HF should at least have plasma levels of B-type natriuretic peptide (BNP) of 100pg/ml to confirm the diagnosis of HF.[6,7] The inclusion of this criterion in the guidelines may be a first step to diagnose HF-PEF easier, and differentiate between patients with HF and patients with other conditions. Nevertheless, in clinical practice, determination of plasma levels of BNP is still not standardized, and specialists are confronted with many patients complaining of severe symptoms of exercise intolerance, breathlessness, and poor quality of life despite a 'normal' ejection fraction. These patients are still largely ignored, under diagnosed, and under treated.[8] Therefore, there is a need to better define, understand and treat HF-PEF.[8]

However, due to the inclusion of having a plasma BNP-level>100pg/ml to meet the diagnostic criteria of HF or HF-PEF, a group of patients with HF symptoms, a preserved ejection fraction and BNP-levels<100pg/ml do not meet the HF diagnostic criteria anymore. Except for their BNP-levels, there is no knowledge on how these patients differ from patients with HF-PEF and BNP-levels>100pg/ml,

and how they would be diagnosed and treated now. Therefore, in order to gain more insight in the characteristics of patients with a preserved ejection fraction and BNP-levels<100pg/ml, we compared patient characteristics, HF symptoms and QoL measurements of these patients to patients with HF-PEF and BNP-levels higher than 100pg/ml.

2. Methods

2.1 Patient population

Data were collected as part of the COACH study (Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure). COACH was a multicenter, randomized clinical trial on the effect of a disease management program in HF, the design and main results have been published.[9,10] In short, 1023 patients from 17 hospitals in the Netherlands were enrolled in the COACH study. Patients were included in the study during a hospitalization for HF (NYHA functional class II to IV), with HF as the primary diagnosis. The diagnosis was based on a combination of typical signs and symptoms according to the ESC guidelines[11] for which a hospital stay was considered necessary. During hospitalization all patients received standard care, both pharmacological and non-pharmacological, according to the guidelines in a cardiology ward, staffed by cardiologists and registered nurses.[11] Patients were 18 years or older and had evidence of structural underlying heart disease. Exclusion criteria were: concurrent inclusion in a study requiring additional visits to research health care personnel; restrictions that made the patient unable to fill in data collection forms; invasive intervention within the last 6 months or planned during the following 3 months; or ongoing evaluation for heart transplantation. All patients gave written informed consent.

In the current study only patients with an LVEF ≥40%, with complete data on BNP-levels and all QoL instruments were included. The study was performed in accordance with the principles outlined in the Declaration of Helsinki and was approved by the Medical Ethics Committee in each participating centre.

2.2 Left ventricular ejection fraction and brain natriuretic peptide

Data on left ventricular function (LV function) were obtained by standard trans-thoracic echocardiography. These data were used to define HF-PEF as having an LVEF ≥40%. Plasma BNP levels were determined within 4h of blood collection (1ml blood, collected in EDTA), on the day of hospital discharge or on the day before hospital discharge. All BNP measurements were performed using a fluorescence immunoassay kit (Triage®; Biosite Incorporated, San Diego, CA, USA).[12]

2.3 Quality of life

Data on QoL were collected during hospitalization. Quality of life was assessed in three different ways: global well-being, disease generic QoL and disease specific QoL.

Global well-being was assessed by Cantril's Ladder of Life. This is a single-item measure which asks the patient to rate their sense of well being on a ladder, with 10 reflecting the best possible life imaginable and 0 reflecting the worst possible life imaginable. Cantril's Ladder of Life has been used in various cardiovascular studies and is considered to be a valid measure of global well-being.[13] A higher score indicates better well being.[14]

Disease generic QoL was assessed by the Medical Outcome Study 36-item General Health Survey (RAND36), a self-report questionnaire of general health status and comparable to the Short-Form-36 Health Survey (SF-36).[15,16] The RAND36 is a well-validated generic, 36-item questionnaire that includes 9 health concepts that represent dimensions of QoL: physical functioning, social functioning, role limitations because of physical functioning, role limitations because of emotional functioning, mental health, vitality, bodily pain, general health and perceived health change. Each dimension has a score between 0 and 100; a higher score means better health.[15]

Disease specific QoL was measured with the Minnesota Living with Heart Failure questionnaire (MLwHFQ).[17] The MLwHFQ is a 21-item scale assessing how and to what extent HF has affected the life of the respondent during the last month.

The MLwHFQ has a scoring range of zero for no impairment to 105 for maximum impairment as a result of HF. The questions cover symptoms and signs relevant to HF, e.g. physical activity, social interaction, sexual activity, work and emotions. Three scores can be determined: an overall score (21 items, 0-105), the physical dimension (8 items, 0-40) and the emotional dimension (5 items, 0-25). Higher MLwHFQ scores mean a worse QoL.

Symptoms of HF were assessed from an interview comprising ten structured questions. During this interview, patients were asked whether they had experienced the following symptoms during the last month: ankle oedema during the day, ankle oedema when getting out of bed in the morning, sleep disturbance, fatigue, breathlessness at rest and during exertion, orthopnoea, coughing, dry cough or loss of appetite. These ten symptoms were clustered in six symptom indexes: oedema, sleep disturbance, fatigue, dyspnoea, coughing and loss of appetite. A total HF symptom score was obtained from the sum of the six symptom indexes.[18]

2.4 Statistical analyses

Descriptive statistics were used to characterize the study population. Data are presented as means ± standard deviations or percents. Student's t-tests and Mann Whitney tests for continuous variables and Chi square tests for categorical variables were performed to compare demographic characteristics, clinical characteristics, QoL and HF symptoms between patients with low BNP-levels (BNP<100pg/ml) and high BNP-levels (BNP>100 pg/ml).

Analyses were performed using PASW Statistics for windows version 18 (SPSS Inc., Chicago, USA). Outcomes were considered statistically significant when $p<0.05$.

3. Results

3.1 Patient characteristics

Of the 1023 patients included in the main COACH study, 199 patients had an LVEF ≥40% and complete data on BNP-levels and all QoL instruments. Patients had a mean age of 73 (± 10), 54% was male, had a mean LVEF of 51% (± 9%) and the median of the BNP-levels was 305pg/ml (Inter Quartile Range (IQR) 132-763pg/ml). Of the 199 patients with an LVEF ≥40%, 37 had BNP-levels lower than 100pg/ml (19%). Significantly more patients with low BNP-levels were classified as NYHA functional class III-IV than patients with high BNP-levels (60% vs. 38%, p=0.016). Patients with low BNP-levels were more often obese (47% vs. 24%, p=0.007), were less often treated with beta-blockers and diuretics (resp. 35% vs. 65%, p=0.001 and 87% vs. 98%, p=0.001), and had a higher mean LVEF (54% vs. 50%, p=0.003) than patients with high BNP-levels (Table 1). They did not differ from the patients with high BNP-levels on co-morbidities like COPD, diabetes and anaemia.

Table 1. Characteristics of patients with LVEF ≥40%

	All patients (n=199)	BNP<100 pg/ml (n=37)	BNP>100 pg/ml (n=162)	p-value*
Age	73 ± 10	72 ± 9	73 ± 10	.548
Gender (male)	54%	54%	57%	.762
NYHA III/IV	42%	60%	38%	.016
LVEF %	51 ± 9	54 ± 10	50 ± 8	.003
BNP (pg/mL) median (IQR)	305 (132-763)	51 (28-73)	433 (227-836)	<.001
Heart rate (bpm)	72 ± 13	73 ± 12	72 ± 13	.835
Systolic blood pressure (mmHg)	125 ± 23	127 ± 23	124 ± 23	.533
Diastolic blood pressure (mmHg)	69 ± 12	73 ± 14	68 ± 12	.050
Ischemic heart failure	59%	65%	57%	.406
Haemoglobin (mmol/L)	8.3 ± 1.3	8.5 ± 1.2	8.3 ± 1.2	.404
Co-morbidities				
Anaemia**	32%	24%	34%	.258
COPD	32%	35%	32%	.668
Asthma	4%	5%	4%	.634
Obese (BMI>30 kg/m²)	29%	47%	24%	.007
Diabetes	31%	32%	30%	.795
Hypertension	49%	60%	50%	.168
Atrial fibrillation	51%	49%	52%	.725
Medication				
ACE/ARB	79%	81%	78%	.718
Beta-blockers	60%	35%	65%	.001
Diuretics	96%	87%	98%	.001

* Comparison between patients with BNP<100 pg/ml and BNP>100 pg/ml
** Diagnosis anaemia: females Hb<7.5 mmol/l, males Hb<8.1 mmol/l
Abbreviations: LVEF=left ventricular ejection fraction; BNP=B-type Natriuretic peptide; IQR=Inter Quartile Range; NYHA=New York Heart Association; COPD=Chronic Obstructive Pulmonary Disease; ACE=Angiotensin Converting Enzyme; ARB=Angiotensin Receptor Blocker;

3.2 Symptoms of heart failure

Patients reported on average four symptoms of HF. Most reported symptoms of HF were dyspnoea (97%) and fatigue (88%). More than two third of the patients had oedema (67%) and sleep disturbance (68%). Sixty-two percent reported coughing and 49% loss of appetite. Patients with low BNP-levels did not differ on reported symptoms from patients with high BNP-levels, except for loss of appetite, which was less often reported by patients with low BNP-levels (33% vs. 52%) (Table 2).

3.3 Quality of life

The mean score on global wellbeing, as measured with Cantril's Ladder of Life, in the total group was 6.2, and did not differ significantly between HF-PEF patients with low BNP-levels and high BNP-levels (Table 2).

Mean scores of all dimensions of the RAND36 in the total group varied between 18 and 67 on the theoretical range between 0-100, with the lowest scores for role limitations physical (18 ± 33), health change (26 ± 23) and physical functioning (33 ± 26), and highest scores on mental health (67 ± 21) and bodily pain (63 ± 34). There were no significant differences on the QoL dimensions of the RAND36 between patients with low and high BNP-levels (Table 2). However, there was a clinical relevant difference (mean scores differed more than 5 points)[19] in on the physical functioning, general health and bodily pain dimensions of the RAND36, in which patients with low BNP-levels had worse QoL compared to patients with high BNP-levels.

The mean score of all patients on the total scale of the MLwHFQ was 44. On the physical and emotional subscales, mean scores were 23 and 6, respectively. The MLwHFQ total scores, as well as the physical and emotional subscale scores did not differ significantly between patients with low and high BNP-levels (Table 2).

Table 2. Quality of life in patients with LVEF ≥40%

	All patients (n=199)	BNP<100 pg/ml (n=37)	BNP>100 pg/ml (n=162)	p-value*
Ladder of Life				
Well-being	6.2 ± 1.8	6.0 ± 2.0	6.2 ± 1.8	.435
RAND-36[a]				
Physical functioning	33 ± 25	27 ± 22	35 ± 26	.082
Social functioning	57 ± 32	60 ± 31	57 ± 33	.588
Role limitations Physical	18 ± 33	18 ± 33	18 ± 34	.984
Role limitations Emotional	53 ± 46	52 ± 48	53 ± 46	.942
Mental Health	67 ± 21	66 ± 22	67 ± 21	.775
Vitality	40 ± 22	37 ± 24	40 ± 22	.410
Bodily Pain	63 ± 34	59 ± 34	64 ± 34	.417
General Health	44 ± 19	39 ± 19	45 ± 19	.092
Health Change	26 ± 23	24 ± 22	26 ± 23	.619
Minnesota Living with Heart Failure[b]				
Total	42 ± 21	44 ± 21	41 ± 21	.353
Physical	23 ± 11	23 ± 9	23 ± 11	.737
Emotional	6 ± 6	8 ± 7	6 ± 6	.097
Symptoms				
Oedema	67%	78%	65%	.112
Dyspnoea	97%	100%	96%	.197
Cough	62%	54%	64%	.251
Sleep disturbance	68%	62%	70%	.370
Loss of appetite	49%	33%	52%	.044
Fatigue	88%	89%	88%	.796
Total number of symptoms (0-6)	4.3 ± 1.3	4.2 ± 1.4	4.3 ± 1.2	.533

* Comparison between patients with BNP<100 pg/ml and BNP>100 pg/ml

[a] A higher score means better health

[b] A lower score means better health

4. Discussion

The main finding of our study is that a group of patients presenting with HF symptoms who would, based on the current guidelines exclusively due to their BNP-levels, not be diagnosed with HF, are at least as much suffering from their conditions as patients who do meet the diagnostic criteria of HF. These patients with a preserved ejection fraction and BNP-levels<100pg/ml, do not differ from patients with HF-PEF and BNP-levels>100pg/ml on a broad range of characteristics and HF symptoms, except for that they are more often obese and in NYHA III-IV. Furthermore, they have a similarly impaired QoL as patients with HF-PEF and BNP-levels>100pg/ml, although there is a clinically relevant difference[19] in the scores resulting in a worse physical functioning, general health, and bodily pain in patients with low BNP-levels.

Heart failure with preserved ejection fraction (HF-PEF) is increasingly recognized as a major public health problem. Although, there is growing interest in reporting data on HF-PEF, there is limited understanding pathology of HF-PEF. It is even uncertain whether HF-PEF is truly HF, or whether symptoms are a result of comorbidities that are highly prevalent in the elderly, such as renal dysfunction, anaemia, and lung disease.[20,21] Another widely discussed issue concerns the diagnosis of HF-PEF.[21] The HF guidelines of 2008 introduced a requirement of plasma BNP-levels>100pg/ml for diagnosing HF, in addition to presence of HF symptoms.[6,7] Resulting in that patients with HF symptoms but with BNP-levels<100pg/ml do not have HF, but actually suffer from another condition. Therefore, it is expected that the prevalence of comorbidities among this patient population would be higher than in patient with high BNP-levels. However, there are no studies on differences in characteristics from the patients with higher BNP-levels, and their possible diagnose. Our results show no differences between both patient groups in comorbidities, except for obesity. It is known that plasma BNP-levels decrease in obese patients,[22,23] which might suggest that these patients still suffer from HF-PEF, despite their lower plasma BNP-levels. Furthermore, they do not differ in the reported HF symptoms, except for loss of appetite, which is less often reported in patients with low BNP-levels, but could be explained by the

high number of obese patients in the sample. We did find that these patients are worse off when it comes to NYHA functional class. They are significantly more often in NYHA III-IV than patients with high BNP-levels, which means they have a lower endurance and are faster short of breath. Although, these patients, based on the current guidelines, would not be diagnosed with HF, they are at least as much suffering from their conditions as patients who would be diagnosed with HF. However, the diagnosis of these patients remains unclear, resulting in a dilemma for the clinical practice when it comes to who should treat these patients. Like patients with HF-PEF, their physical functioning is low, and regardless of possible pharmacological treatment, these patients could definitely benefit from exercise treatment, and referral to a rehabilitation centre would be advised.[24,25]

The findings of the current study raise important questions regarding the use of plasma BNP-levels as a biomarker for the diagnoses of HF-PEF. Yamamoto *et al.* already stated that we should be cautious in using BNP alone to diagnose HF-PEF, because concentrations of BNP increase in normal older and/or female individuals, and in those with renal dysfunction and atrial fibrillation, and decreases in obese subjects.[26] Due to individual changes in plasma BNP-levels it could be suggested to measure BNP-levels serially and use changes in BNP-levels over time, in stead of a single measurement, to diagnose HF-PEF.[27] Although BNP-levels have a powerful prognostic value on mortality and morbidity,[28] the diagnostic value of this biomarker might be debated. The numerous studies on finding new biomarkers for diagnosing HF-PEF seem to confirm this.[29-31]

Several limitations of this study should be considered. First, the sample size was small. However, in the current literature data on differences between HF-PEF patients with high and low BNP are not available, and regardless the sample size, we did find significant differences. This warrants confirmation of our findings in a larger population, and probably statistical trends found in our study, might become significant in a larger study population. Secondly, we defined HF-PEF as an LVEF ≥40%. Nowadays, the cut-off point of LVEF to diagnose HF-REF or HF-PEF is still a matter of debate. We chose a cut-off of 40% because it has been used in other large studies.[32]

In conclusion, patients with a preserved ejection fraction and plasma BNP-levels<100 pg/ml have the same characteristics, the same comorbidities, the same HF symptoms, and a similarly impaired QoL as patients with a preserved ejection fraction and BNP-levels>100pg/ml, except for that they are more often obese, which is known to decrease BNP-levels.

References

1. Paulus WJ, van Ballegoij JJ. Treatment of heart failure with normal ejection fraction: an inconvenient truth! *J Am Coll Cardiol* 2010;**55**:526-537.
2. Kindermann M, Reil JC, Pieske B, van Veldhuisen DJ, Böhm M. Heart failure with normal left ventricular ejection fraction: what is the evidence? *Trends Cardiovasc Med* 2008;**18**:280-292.
3. Jaarsma T, Halfens R, Abu-Saad HH, Dracup K, Stappers J, van Ree J. Quality of life in older patients with systolic and diastolic heart failure. *Eur J Heart Fail* 1999;**1**:151-160.
4. Hoekstra T, Lesman-Leegte I, van Veldhuisen DJ, Sanderman R, Jaarsma T. Quality of life is impaired similarly in heart failure patients with preserved and reduced ejection fraction. *Eur J Heart Fail* 2011;**13**:1013-1018.
5. Lam CS, Donal E, Kraigher-Krainer E, Vasan RS. Epidemiology and clinical course of heart failure with preserved ejection fraction. *Eur J Heart Fail* 2011;**13**:18-28.
6. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. *Eur J Heart Fail* 2008;**10**:933-989.
7. McMurray JJ, Adamopoulos S, Ander SD, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2012 [epub ahead of print].
8. Pieske B. Heart failure with preserved ejection fraction-a growing epidemic or 'The Emperor's New Clothes?' *Eur J Heart Fail* 2011;**13**:11-13.

9. Jaarsma T, Van Der Wal MH, Hogenhuis J, et al. Design and methodology of the COACH study: a multicenter randomised Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure. *Eur J Heart Fail* 2004; **6**:227-233.
10. Jaarsma T, van der Wal MH, Lesman-Leegte I, et al. Effect of moderate or intensive disease management program on outcome in patients with heart failure: Coordinating Study Evaluating Outcomes of Advising and Counselling in Heart Failure (COACH). *Arch Intern Med* 2008; **168**:316-324.
11. Remme WJ, Swedberg K. Guidelines for the diagnosis and treatment of chronic heart failure. *Eur Heart J* 2001;**22**:1527-1560.
12. Hogenhuis J, Voors AA, Jaarsma T, Hillege HL, Hoes AW, van Veldhuisen DJ. Low prevalence of B-type natriuretic peptide levels <100 pg/mL in patients with heart failure at hospital discharge. *Am Heart J* 2006; **151**:1012e1-1012e5.
13. Jenkins LS, Brodsky M, Schron E, et al. Quality of life in atrial fibrillation: the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Am Heart J* 2005;**149**:112-120.
14. Cantril H. *The pattern of human concerns*. New Brunswick, NJ: Rutgers University Press; 1965.
15. Van der Zee KI, Sanderman R, Heyink JW, de Haes H. Psychometric qualities of the RAND 36-item Health Survey 1.0: a multidimensional measure of general health status. *Int J Behav Med* 1996;**3**:104-122.
16. Ware JE. The SF-36 Health Survey. In: Spilker B, editor. *Quality of life and pharmacoeconomics in clinical trials*. Philadelphia, PA: Raven, 1996. p337-349.
17. Rector TS, Kubo SH, Cohn JN, Patients' self-assessment of their congestive heart failure: content, reliability and validity of a new measure, the Minnesota Living with Heart Failure questionnaire. *Heart Failure* 1987;**3**:198–209.
18. Lesman-Leegte I, Jaarsma T, Sanderman R, Linssen G, van Veldhuisen DJ. Depressive symptoms are prominent among elderly hospitalised heart failure patients. *Eur J Heart Fail* 2006;**8**:634-640.

19. Wyrwich KW, Tierney WM, Babu AN, Kroenke K, Wolinsky FD. A comparison of clinically important differences in health-related quality of life for patients with chronic lung disease, asthma, or heart disease. *Health Serv Res* 2005;**40**:577-591.
20. Bench T, Burkhoff D, O'Connell JB, et al. Heart failure with normal ejection fraction: consideration of mechanisms other than diastolic dysfunction. *Curr Heart Fail Rep* 2009;**6**:57-64.
21. Pieske B. Heart failure with preserved ejection fraction—a growing epidemic or 'The Emperor's New Clothes?' *Eur J Heart Fail* 2011;**13**:11-13.
22. Wang TJ, Larson MG, Levy D, et al. Impact of obesity on plasma natriuretic peptide levels. *Circulation* 2004;**109**:594-600.
23. Clerico A, Giannoni A, Vittorini S, Emdin M. The paradox of low BNP-levels in obesity. *Heart Fail Rev* 2012;**17**:81-96.
24. Pieske B, Edelmann F, Gelbrich G, et al. Exercise training improves exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction. Results of the ex-DHF (exercise training in diastolic heart failure) pilot study. *Am Coll Cardiol* 2011;**58**:1780-1791.
25. Kitzman DW, Brubaker PH, Morgan TM, Stewart KP, Little WC. Exercise training in older patients with heart failure and preserved ejection fraction: a randomized controlled, single-blind trial. *Circ Heart Fail* 2010;3:659-667.
26. Yamamoto K, Sakata Y, Ohtani T, Takeda Y, Mano T. Heart failure with preserved ejection fraction. *Circ J* 2009;**73**:404-410.
27. Anand IS, Fisher LD, Chiang YT, et al. Changes in brain natriuretic peptide and norepinephrine over time and mortality and morbidity in the Valsartan Heart Failure Trial (Val-HeFT). *Circulation* 2003;**107**:1278-1283.
28. Parekh N, Maisel AS. Utility of B-natriuretic peptide in the evaluation of left ventricular diastolic function and diastolic heart failure. *Curr Opin Cardiol* 2009;**24**:155-160.
29. Shuai XX, Chen YY, Lu YS, et al. Diagnosis of heart failure with preserved ejection fraction: which parameters and diagnostic strategies are more valuable? *Eur J Heart Fail* 2011;**13**:737-745.

30. de Boer RA, Lok DJ, Jaarsma T, et al. Predictive value of plasma galectin-3 levels in heart failure with reduced and preserved ejection fraction. *Ann Med* 2011;**43**:60-68.
31. Carrasco-Sánchez FJ, Galisteo-Almeda L, Páez-Rubio I, et al. Prognostic value of cystatin C on admission in heart failure with preserved ejection fraction. *J Card Fail* 2011;**17**:31-38.
32. Lewis EF, Lamas GA, O'Meara E, et al. Characterization of health-related quality of life in heart failure patients with preserved versus low ejection fraction in CHARM. *Eur J Heart Fail* 2007;**9**:83-91.

Chapter 5:
Perceived sexual difficulties and associated factors in patients with heart failure

Tialda Hoekstra, Tiny Jaarsma, Robbert Sanderman, Dirk J. van Veldhuisen, Ivonne Lesman-Leegte

American Heart Journal 2012;163:246-251

Abstract

Background: Sexual dysfunction is a common problem of increasing incidence in patients with heart failure (HF). However, there is no knowledge on which demographic, clinical and quality of life (QoL) aspects are related to difficulties in sexual activity nor on the course of sexual difficulties in patients with HF.

Methods: Data on sexual difficulties were collected at 1 and 18 months after an HF hospitalization (n=792, mean age 69 ± 12; 35% female; mean left ventricular ejection fraction 33% ± 14) by the question on sexuality of the Minnesota living with HF questionnaire. Demographic and clinical factors were assessed from medical records and QoL by Minnesota living with HF questionnaire, Medical Outcome Study 36-item General Health Survey, and Ladder of Life.

Results: In total 48% (n=380) of the patients perceive difficulties in sexual activity at 1 month after discharge, and 70% continued to perceive this at 18 months. Furthermore, 27% of the patients without difficulties at 1 month developed them during follow-up. Living with a partner (OR 3.76, 95% CI 2.58-5.48), younger age (OR 0.96, 95% CI 0.94-0.97)), male gender (OR 3.08, 95% CI 2.10-4.43), overall wellbeing (OR 1.13, 95% CI 1.00-1.27), and physical (OR 1.06, 95% CI 1.06-1.08) and emotional QoL (OR 1.07, 95% CI 1.03-1.10) were independently associated with perceived difficulties in sexual activity.

Conclusions: Perceived difficulties in sexual activity are common in patients with HF, particularly in younger and male patients and continue over time. Patients who perceive difficulties in sexual activity report a significant lower QoL and overall wellbeing than those who do not.

1. Introduction

Heart failure (HF) is a significant health problem affecting the quality of life (QoL) of patients.[1] Patients with HF suffer from symptoms such as fatigue and shortness of breath,[2] psychological factors such as depression,[1,3] and low functional capacity[4,5], and they also need to manage lifestyle changes.[6] These factors affect not only overall QoL, but also the intimacy needs of a patient with HF.[7]

It is often expected that among seriously ill patients sexual activity is not important. However, patients with HF consider sexual activity in their current condition as an essential aspect of QoL,[8] but symptoms of HF do affect the sexual relationships of patients with HF.[9] At least 50% of all patients with HF report that their sexual activity has reduced or completely ceased as a result of their HF. Furthermore, half of the patients with HF have problems with sexual activity caused by erectile dysfunction or orgasmic problems and sexual dissatisfaction.[7-10]

The current HF guidelines recommend counseling on sexual activity with both male and female patients and their partners. The given class of recommendation is I; however, the level of evidence is C, which indicates that counseling on sexual activity is suggested to be very important, but not many studies have focused on this subject.[11] Two small studies examining predictors of decrease in sexual activity in relatively young, and predominantly male patients with HF show that worse functional capacity, high New York Heart Association (NYHA) class, the number of medications, diabetes, as well as tobacco and alcohol use contribute to a decrease of sexual activity.[7,12] Furthermore, HF therapy with beta-receptor blockers, digoxin and thiazide are known to worsen sexual activity.[13] However, it is not known whether these variables are also related to difficulties in sexual activity in an older HF population or specifically in women. In addition, studies on sexual problems in patients without a partner are lacking.

Knowledge on the relationship between difficulties with sexuality and QoL is based on a few smaller studies in specific HF study populations and shows that better sexual function is related to a higher overall wellbeing.[9] To appropriately address the importance and effects of difficulties in sexual activity in the lives of

all patients with HF, including women and elderly, more information is needed on the relationship between QoL and sexual problems.

Although there is a recent growing interest in reporting data on sexual problems of patients with HF, current studies have a cross-sectional design without providing insight in sexual problems over time. In case of sexual problems that are assessed at hospital discharge, clinicians may assume that these will disappear spontaneously during recovery. In general there is little follow-up on the course of sexual activity during the trajectory of HF. Only one small study reported that both at discharge and at 9 months after discharge patients with HF reported problems and sexual concerns. However, this study did not report the development of new cases or recovered patients during this period of time.[9]

To gain more insight in sexual problems in patients with HF, the following research questions were formulated to study in a large representative population of patients with HF:

1. Which demographic and clinical variables are related to difficulties in sexual activity?
2. Which QoL aspects are independently related to difficulties in sexual activity?
3. What is the course of difficulties in sexual activity over time?

2. Methods

2.1 Patient population

Data of patients participating in the COACH (Coordinating study evaluating Advising and Counselling in Heart failure) study were used. The COACH study is a multicenter, randomized clinical trial on the effect of education and counseling in HF.[14,15] Between November 2002 and February 2005, 1023 patients from 17 Dutch hospitals were included in the COACH study. Patients were included in the study during admission for HF (NYHA functional class II to IV), with HF as the primary diagnosis as confirmed by a cardiologist. During hospitalization patients were randomized to (1) basic support, (2) intensive support, or (3) control

treatment. Patients were 18 years or older and had evidence of structural underlying heart disease as shown at cardiovascular imaging. Reasons for exclusion were as follows: concurrent inclusion in a study requiring additional visits to health care personnel, restrictions that made the patient unable to fill in data collection forms, invasive intervention within the last 6 months or planned during the following 3 months, or ongoing evaluation for heart transplantation. All patients gave written informed consent. Patients completed questionnaires and were interviewed by an independent interviewer not involved in care for these patients. All patients were treated from hospital discharge until 18 months afterwards hospital discharge.

The study was performed conform the principles outlined in the Declaration of Helsinki and was approved by the Committee for Ethics in Medical Investigations.

2.2 Data collection

2.2.1 Difficulties with sexual activity

Data on sexual activity in the COACH study were collected during index hospitalization and follow up. To minimize the confounding effect of the recent hospitalization on sexual activity, we used the data on sexual activity at 1 month after discharge. Sexual activity was assessed by the following question of the Minnesota Living with Heart Failure (MLwHF) questionnaire[16]: "Did your heart failure prevent you from living as you wanted during the past month by making your sexual activities difficult"' Scoring format consists of 0 (no difficulties in sexual activity) and 1 to 5 (very little to very much difficulties). For the "course of difficulties in sexual activity", data at 1 and 18 months after discharge were used. Four groups were created based on the scores at the 2 different time points: continued difficulties (at 1 and 18 months difficulties with sexuality); new onset difficulties (no problems at 1 month and problems at 18 months); recovered difficulties (problems at 1 month but not at 18 months), and no difficulties (at 1 and 18 months). Data on sexual activity was also collected at 6 and 12 months after discharge. These data were analyzed as well; however results do not differ

from the current results at 18 months after discharge. For reasons of readability, it was decided not to include these results.

2.2.2 Demographic and clinical characteristics

Data on demographic and clinical characteristics were collected from chart review, interviews and questionnaires. Depressive symptoms were measured with the Center for Epidemiological Studies Depression scale (CES-D), a 20-item self report questionnaire designed to measure depressive symptoms in the general population and has been widely used with the medically ill. A total sum score is used (0-60), with higher scores indicating more depressive symptoms.[17,18]

Functional capacity was measured by the 6-minute walking test (6MWT) on a predefined course. Patients were instructed to walk as many meters as they could within 6 minutes. At standardized moments the instructor told the patients the amount of time remaining. Patients were allowed to stop or slow down if necessary. The 6MWT is a reliable and well validated test for functional capacity in patients with HF.[19]

2.2.3 Quality of life

Data on QoL were collected using several questionnaires completed at 1 month after discharge. Disease specific QoL was measured with the MLwHF questionnaire,[16] a 21-item questionnaire assessing how HF has affected the life of the respondent during the last month. The questions cover symptoms and signs relevant to HF such as physical activity, social interaction, sexual activity, work and emotions. Three scores can be determined: an overall score (21 items, 0-105), the physical dimension (8 items, 0-40) and the emotional dimension (5 items, 0-25). Higher scores mean worse QoL. The item on sexual functioning is in neither one of both dimensions; however it is part of the total score, therefore the total score was excluded from the analyses.

Overall well-being was assessed by Cantril's Ladder of life. This is a single-item measure that asks to rate the sense of well-being on a ladder, with 10 reflecting the

best possible life imaginable and 0 reflecting the worst possible life imaginable. A higher score indicates better well-being.[20]

General QoL was assessed by the Medical Outcome Study 36-item General Health Survey (RAND-36), a self-report questionnaire of general health status. It is a well-validated generic, 36-item questionnaire that includes 9 health concepts that represent dimensions of QoL: physical functioning, social functioning, role limitations because of physical functioning, role limitations because of emotional functioning, mental health, vitality, bodily pain, general health and perceived health change. Each dimension has a score between 0 and 100; a higher score means better QoL.[21]

2.3 Statistical analysis

Data are presented as mean ± SD or as percentages unless stated otherwise. Univariate analyses were carried out by using Mann-Whitney U for continues or Chi^2 for categorical variables. Logistic regression analysis was performed to assess which demographic and clinical variables were independently associated with difficulties in sexual activity. Difficulties in sexual activity was used as the dependent variable. Based on univariate differences with $p<0.10$, the following variables were inserted in the regression model, using backward methods: gender, age, living with a partner, left ventricular ejection fraction (LVEF), CES-D, 6MWT, angiotensin-converting enzyme (ACE)/angiotensin receptor blocker (ARB), diuretics, Ladder of life, MLwHF physical and emotional dimensions, and the following dimensions of the RAND-36: social functioning, physical role limitations, emotional role limitations, mental health, vitality, bodily pain and general health. Student's t-tests were carried out to compare the change in the independently associated QoL scores (score at 18 months minus score at 1 month after discharge) and the number of hospital admissions between new onset patients and patients with no difficulties.

Analyses were performed using SPSS 16 (SPSS Inc., Chicago, USA). Outcomes were considered statistically significant when $p<0.05$.

The COACH study was supported by a program grant from the Netherlands Heart Foundation (grant 2000Z003). Additional unrestricted grants for the main COACH study were obtained from Biosite Europe, France, Roche Diagnostics, The Netherlands and Novartis Pharma BV, The Netherlands. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

3. Results

3.1 Patients

Of the 1023 patients included in the COACH study, 44 died within 1 month after discharge. Of the survivors, 792 (81%) patients completed the question about sexuality of the MLwHF questionnaire at 1 month after discharge (mean age 69 (± 12); 35% female; mean LVEF 33% (± 14)). The 187 patients who did not complete this question were significantly more often female, older, living without a partner, in NYHA III to IV at discharge, diagnosed with diabetes, had a higher LVEF and walked less far on the 6MWT. Of the 187 patients who survived the follow-up at 1 month after discharge, but specifically did not complete the question on sexual difficulty, 51 patients did fill out the rest of the MLwHF questionnaire.

At 18 months after discharge, 638 (81%) of the 792 patients were alive and 555 (87%) patients completed the question on sexual activity both at 1 and 18 months after discharge.

Table 1. Characteristics of patients with and without difficulties in sexual activity

	No difficulties (n=412)	With difficulties (n=380)	p-value
Demographics			
Gender (female)	46%	24%	<.001
Age	72 ± 11	66 ± 12	<.001
Living with a partner	49%	82%	<.001
Clinical characteristics			
Support			
Care as usual	33%	33%	.819
Basic support	32%	34%	
Intensive support	36%	33%	
NYHA III-IV	46%	48%	.514
LVEF %	35 ± 15	32 ± 14	.007
Ischemic heart failure	39%	42%	.536
Myocardial infarction	41%	42%	.928
Hystory of atrium fibrilation	42%	42%	.919
Hypertension	44%	40%	.329
Diabetes	29%	24%	.100
COPD	25%	26%	.743
BNP (pg/mL) median (IQR)	400 (180-808)	427 (194-888)	.272
BMI	27 ± 5	27 ± 5	.244
Smoking	11%	14%	.339
Length of disease (years)	2.6 ± 4.5	2.4 ± 3.8	.131
CES-D (discharge)	15 ± 11	16 ± 11	.035
6 min walk test distance (m)	244 ± 137	272 ± 134	.013
Medication			
ACE/ARB (discharge)	83%	88%	.019
Betablockers (discharge)	66%	71%	.147
Diuretics (discharge)	94%	97%	.072

Abbreviations: NYHA=New York Heart Association; LVEF=Left Ventricular Ejection Fraction; COPD=Chronic Obstructive Pulmonary Disease; BNP=B-type Natriuretic peptide; IQR=Inter Quartile Range; BMI=Body Mass Index; CES-D= Center for Epidemiological Studies Depression Scale; ACE=Angiotensin Converting Enzyme; ARB=Angiotensin Receptor Blocker

3.2 Difficulties with sexual activity

Of the 792 patients, 380 (48%) reported difficulties in sexual activity at one month after discharge. Almost half of these patients (n=186) reported considerable difficulties, they reported that HF prevented them *very much* of living as they wanted by making their sexual activities difficult.

Patients with HF who perceive sexual difficulties were more often male (76% vs. 54%, p<0.001), younger of age (66 vs. 72 years old, p<0.001) and more often living with a partner (82% vs. 49%, p<0.001), had a lower LVEF (32% vs. 35%, p=0.007), had a higher score on a depression scale (16 vs. 15, p=0.035) and walked further on the 6MWT (272m vs. 244m, p=0.013) (Table 1). At hospital discharge more patients reporting sexual difficulties had a prescription of ACE/ARB (88% vs. 83%, p=0.019). No differences were found regarding beta-blocker use and the assigned COACH intervention.

Patients with sexual difficulties had significant lower QoL compared to patients without sexual difficulties on both the physical and emotional dimensions of the MLwHF questionnaire (23 vs. 17 and 9 vs. 6, p<0.001) (Table 2). Of 9 dimenstions of the RAND-36, 6 differed significantly between the patients with and without difficulties in sexual activity. Patients who perceive difficulties had significant lower QoL scores on social functioning, physical and emotional role limitations, mental health, vitality and general health.

In multivariate analyses, living with a partner (OR 3.76, 95%, CI 2.58-5.48), younger age (OR 0.96, 95% CI 0.94-0.97)), male gender (OR 3.08, 95% CI 2.10-4.43), overall wellbeing (OR 1.13, 95% CI 1.00-1.27), and physical (OR 1.06, 95% CI 1.06-1.08) and emotional QoL (OR 1.07, 95% CI 1.03-1.10) were independently associated with difficulties in sexual activity caused by HF that prevented patients from living as they wanted (Table 3).

Table 2. Quality of life scores of patients with and without difficulties in sexual activity

	No difficulties (n=412)	With difficulties (n=380)	p-value
Ladder of life			
Well-being	6.4 ± 1.6	6.2 ± 1.6	.068
Minnesota living with Heart Failure			
Physical dimension	17 ± 11	23 ± 11	<.001
Emotional dimension	6 ± 6	9 ± 6	<.001
RAND-36			
Physical functioning	44 ± 28	41 ± 26	.152
Social functioning	61 ± 30	52 ± 29	<.001
Role limitations Physical	26 ± 37	15 ± 30	<.001
Role limitations Emotional	54 ± 46	41 ± 45	<.001
Mental health	72 ± 20	67 ± 21	.002
Vitality	51 ± 23	44 ± 22	<.001
Bodily pain	75 ± 28	72 ± 29	.066
General health	46 ± 20	42 ± 18	.008
Health change	35 ± 28	33 ± 31	.173

Table 3. Adjusted associations between patients with and without difficulties in sexual activity

		95% CI for Odds Ratio			
Variables	*B* (SE)	OR	Lower	Upper	p-value
Age	-.04 (0.01)	.96	.94	.97	<.001
Gender (male)	1.13 (0.20)	3.08	2.10	4.43	<.001
Living with a partner	1.32 (0.19)	3.76	2.58	5.48	<.001
Minnesota living with heart failure-Physical dimension	-.06 (0.01)	1.06	1.04	1.08	<.001
Minnesota living with heart failure-Emotional dimension	-.06 (0.00)	1.07	1.03	1.10	<.001
Ladder of life	.12 (0.06)	1.13	1.00	1.27	.049

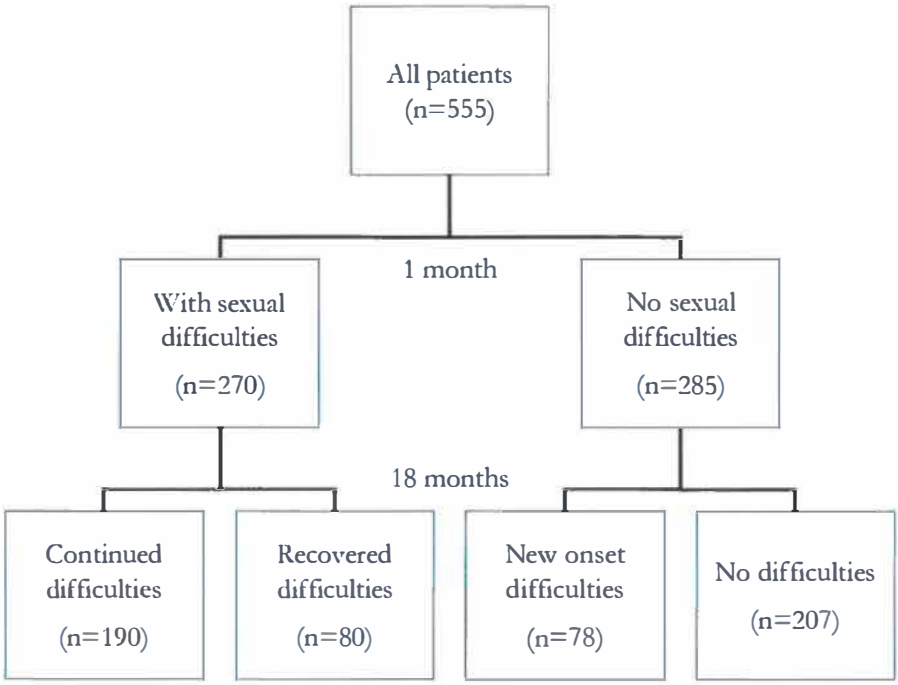


Figure 1. Flowchart of patients and course of perceived difficulties in sexual activity.

3.3 Course of difficulties in sexual activity

At 1 month after discharge, 270 of the 555 patients (49%) reported difficulties in sexual activity, and at 18 months after discharge, 268 (48%) patients reported difficulties in sexual activity in some degree. Analyses over time show that of the 270 patients who reported sexual difficulties at 1 month after discharge, 80 patients (30%) recovered at 18 months follow up and 190 (70%) patients still reported difficulties. Of the 285 patients who did not report sexual difficulties at baseline, 207 (73%) did not report difficulties at 18 months as well, and 78 (27%) developed difficulties during 18 months follow up (new onset difficulties) (Figure 1). Compared to patients without difficulties, patients who developed sexual

difficulties were more often male (55% vs. 78%, p<0.001) and living with a partner (44% vs. 74%, p<0.001). Furthermore, patients who remained without difficulties, improved in QoL over time compared to new onset patients whose QoL scores did not change or worsened (change scores physical QoL -3.5 vs. 0.9, p=0.001, change scores emotional QoL: -2.2 vs. 0.04, p=0.002, changes scores wellbeing: 0.42 vs. -0.01, p=0.047). The number of hospital admissions did not differ between both groups (0.24 vs. 0.32, p=0.376).

4. Discussion

To our knowledge, this is the first study to explore the relationship between perceived difficulties in sexual activity caused by HF and a considerable number of demographic variables, clinical variables, and QoL aspects and reports the course of difficulties in sexual activity, in a representative population of patients with HF. Almost 50% of patients with HF perceive difficulties in sexual activity due to their disease, and most (70%) of these patients continued to report difficulties after an 18 month recovery period. This was a remarkable difference with perceived difficulties experienced by 20% to 30% of healthy older people.[22]

Male gender, younger age, and living with a partner were independently associated with perceived sexual difficulties. Patients who reported difficulties in sexual activity had significant lower disease-specific QoL and overall well-being compared with patients who did not perceive sexual difficulties. We did not find an independent relation of difficulties in sexual activity to disease severity markers such as NYHA, LVEF or B-type natriuretic peptide, or beta blocker use. In addition, the use of tobacco or alcohol, having diabetes, and number of medications, as described in other studies, were not found to be related to sexual activity,[9,12] possibly because of an older and larger study population.

We believe that the present analysis is clinically relevant and extends previous studies by using a large group of older male and female patients with HF. Previous studies assessing the relationship between patient characteristics and sexual functioning used small and predominantly male patient groups.[9,12]

Our study is also unique in the sense that we chose to include both patients with and without a partner. Of course, we realize that having a partner is strongly associated with the perception of sexual problems, because patients who have a partner can be expected to be confronted more often with those problems as part of their daily life.[23] However, our study also showed that 18% of the patients who perceived difficulties with sexual activity were living without a partner; thus, not only patients with a partner experience sexual difficulties caused by HF that prevent them from living as they want. It is important to report the prevalence in dysfunction in both patients with and without a partner, because patients might define sexual activity broader than having intercourse (eg, masturbation) and single patients might worry about their (future) sex life. The second strongest variable related to difficulties in sexual activity was male gender. Of the patients who perceived difficulties in sexual activity, 76% was male. Endothelial dysfunction is prevalent in patients with HF and one of the main common denominators for erectile dysfunction, but not in female sexuality.[8,24] Therefore problems in sexuality can be assumed to affect the male sexual function more than female sexual function. Although previous research mainly focused on male sexuality and erectile dysfunction,[8] our study shows that 24% of the patients who perceive difficulties in sexual activity are women. Heart failure symptoms such as dyspnea, fatigue, and exercise intolerance can be assumed to affect sexuality in both male and female patients.

We rather uniquely report on the course of perceived difficulties with sexual activities. We found that, at both time points, approximately half of the patients reported difficulties with sexual activities caused by symptoms of HF. However, we also demonstrated that 30% of the patients, who reported difficulties at 1 month after discharge, did not report difficulties in sexual activity at follow up. Possible reasons for the decrease in difficulties might be stabilization of HF, increased physical capacity during recovery, or possible use of PDE5 inhibitors. However, at the same time, we found that 27% of the patients without difficulties at 1 month after discharge did perceive sexual problems at 18 months follow-up and that, in 70% of the patients with difficulties, these difficulties remained.

Patients who continue to be without difficulties improved in QoL over time, in contrast to new onset patients, whose QoL stayed the same or worsened. These findings emphasize that sexual concerns need to be discussed more than once during treatment and should become an integral part of HF management and patient education.[25,26] It is known that, although the most of the health care providers feel a responsibility to discuss sexual concerns with their patients, many do not address these concerns in their daily practice.[27,28]

Several limitations of this study should be considered. First, perceiving difficulties in sexual activity was based on a single question from a larger QoL questionnaire. This results in a global measurement of difficulties in sexual activity. However, our results are comparable with studies that used more extensive questionnaires on sexual functioning.[9] Second, the specific question on sexual activity concerns perceived difficulties with sexuality because of HF and that prevents them from living as they want. We do not know if these patients actually have sexual problems, we only know that their HF affects their sexuality. Sexual activity could, for example, be affected by HF symptoms such as fatigue or dyspnea, which is not stated as an actual sexual problem. Therefore, we do not know if these patients actually have sexual problems, for example, problems with erection, or that other factors, such as HF symptoms, make their sexual activities difficult and prevent them from living as they want. When interpreting the results, it should also be taken into account that not necessary patients who are male, living with a partner, and younger of age actually have more difficulties in sexuality. It can be expected that these characteristics are associated with a higher likelihood of reporting difficulties with sexual activities that prevent the person from living as he/she wants. Finally, our findings show that difficulties in sexual activity are related to QoL. Our data do not provide insight in the cause and effect in this relationship. Patients with difficulties in sexual activity can be expected to have a lower QoL, because of these difficulties. However, one can also imagine that a worse QoL can influence sexual relations because of functional impairment and emotional problems.

This study provides an important step toward understanding the occurrence of sexual problems in patients with HF. Perceiving difficulties in sexual activity caused by HF and preventing patients from living as they wanted affect many patients with HF. Furthermore, these difficulties continue over time and influence the QoL of these patients. Therefore, it is of great importance to counsel patients with HF repeatedly on sexual activity during their treatment.

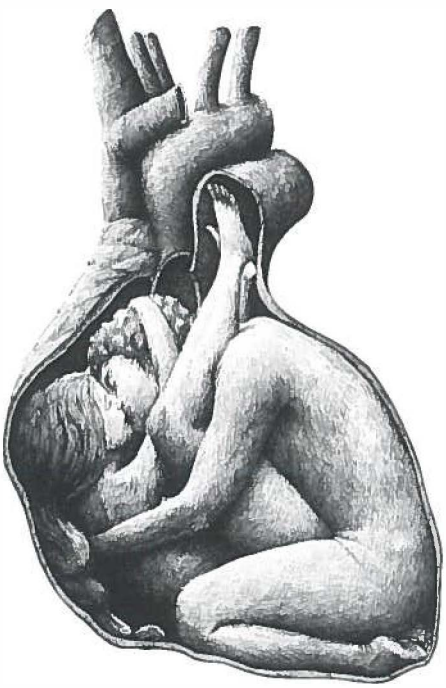
References

1. Lesman-Leegte I, Jaarsma T, Coyne JC, Hillege HL, Van Veldhuisen DJ, Sanderman R. Quality of life and depressive symptoms in the elderly: a comparison between patients with heart failure and age- and gender-matched community controls. *J Card Fail* 2009;**15**:17-23.
2. Jaarsma T, Halfens R, Abu-Saad HH, Dracup K, Stappers J, van Ree J. Quality of life in older patients with systolic and diastolic heart failure. *Eur J Heart Fail* 1999;**1**:151-160.
3. Jaarsma T, Lesman-Leegte I, Hillege HL, Veeger NJ, Sanderman R, van Veldhuisen DJ. Depression and the usefulness of a disease management program in heart failure: insights from the COACH (Coordinating study evaluating Outcomes of Advising and Counseling in Heart failure) study. *J Am Coll Cardiol* 2010;**55**:1837-1843.
4. Smart N, Haluska B, Jeffriess L, Marwick TH. Exercise training in systolic and diastolic dysfunction: effects on cardiac function, functional capacity, and quality of life. *Am Heart J* 2007;**153**:530-536.
5. Winkelmann ER, Chiappa GR, Lima CO, Viecili PR, Stein R, Ribeiro JP. Addition of inspiratory muscle training to aerobic training improves cardiorespiratory responses to exercise in patients with heart failure and inspiratory muscle weakness. *Am Heart J* 2009;**158**:768.e1-768.e7.
6. Van der Wal MH, Jaarsma T, van Veldhuisen DJ. Non-compliance in patients with heart failure; how can we manage it? *Eur J Heart Fail* 2005;**7**:5-17.
7. Jaarsma T, Dracup K, Walden J, Stevenson LW. Sexual function in patients with advanced heart failure. *Heart Lung* 1996;**25**:262-270.
8. Schwarz ER, Kapur V, Bionat S, Rastogi S, Gupta R, Rosanio S. The prevalence and clinical relevance of sexual dysfunctioning in women and men with chronic heart failure. *Int J Impot Res* 2008;**20**:85-91.
9. Jaarsma T. Sexual problems in heart failure patients. *Eur J Cardiovasc Nurs* 2002;**1**:61-67.

10. Westlake C, Dracup K, Walden JA, Fonarow G. Sexuality op patients with advanced heart failure and their spouses or partners. *J Heart Lung Transplant* 1999;**18**:1133-1138.
11. Dickstein K, Cohen-Solal A, Filippatos G et al. ESC Guidelines for the diagnoses and treatment of acute and chronic heart failure 2008. *Eur J Heart Fail* 2008;**29**:2388-2442.
12. Steinke EE, Mosack V, Wright DW, Chung MI., Moser DK. Risk factors as predictors of sexual activity in heart failure. *Dimens Crit Care Nurs* 2009;**28**:123-129.
13. Schwarz ER., Rastogi S, Kapur V, Sulemanjee N, Rodriguez JJ. Erectile dysfunction in heart failure patients. *J Am Coll Cardiol* 2006;**48**:1111-1119.
14. Jaarsma T, Van Der Wal MH, Hogenhuis J, et al. Design and methodology of the COACH study: a multicenter randomised Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure. *Eur J Heart Fail* 2004;**6**:227-233.
15. Jaarsma T, van der Wal MH, Lesman-Leegte I, et al. Effect of moderate or intensive disease management program on outcome in patients with heart failure: Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH). *Arch Intern Med* 2008;**168**:316-324.
16. Rector TS, Kubo SH, Cohn JN. Patients' self-assessment of their congestive heart failure: content, reliability and validity of a new measure, the Minnesota Living with Heart Failure questionnaire. *Heart Failure* 1987;**3**:198–209.
17. Radloff L. The CES-D scale. A self-report depression scale for research in the general population. *Appl Psychol Measure* 1977;**1**:385-401.
18. Schroevers MJ, Sanderman R, Sonderen E van, Ranchor AV. The evaluation of the Center for Epidemiologic Studies Depression (CES-D) scale: depressed and positive affect in cancer patients and healthy reference subjects. *Qual Life Res* 2000;**9**:1015-1029.

19. Demers C, McKelvie RS, Negassa A, Yusuf S. Reliability, validity, and responsiveness of the six-minute walk test in patients with heart failure. *Am Heart J* 2001;**142**:698-703.
20. Cantril H. *The pattern of human concerns*. New Brunswick, NJ: Rutgers University Press; 1965.
21. Van der Zee KI, Sanderman R, Heyink JW, de Haes H. Psychometric qualities of the RAND 36-item Health Survey 1.0: a multidimensional measure of general health status. *Int J Behav Med* 1996;**3**:104-122.
22. Lindau ST, Schumm LP, Laumann EO, Levinson W, O'Muircheartaigh CA, Waite LJ. A study of sexuality and health among older adults in the United States. *N Engl J Med* 2007;**357**:762-774.
23. Dalteg T, Benzein E, Fridlund B, Malm D. Cardiac disease and its consequences on the partner relationship: A systematic review. *Eur J Cardiovasc Nurs* 2011;**10**:140-149.
24. Stein RA. Endothelial dysfunction, erectile dysfunction, and coronary heart disease: the pathophysiologic and clinical linkage. *Rev Urol* 2003;**5**(Suppl 7):S21-S27.
25. Lainscak M, Blue L, Clark AL, et al. Self-care management of heart failure: practical recommendations from the Patient Care Committee of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2011;**13**:115-126.
26. McDonagh TA, Blue L, Clark AL, et al. European Society of Cardiology Heart Failure Association Standards for delivering heart failure care. *Eur J Heart Fail* 2011;**13**:235-241.
27. Jaarsma T, Strömberg A, Fridlund B, et al. Sexual counselling of cardiac patients: nurses' perception of practice, responsibility and confidence. *Eur J Cardiovasc Nurs* 2010;**9**:24-29.
28. Jaarsma T, Steinke EE, Gianotten WL. Sexual problems in cardiac patients: how to assess, when to refer. *J Cardiovasc Nurs* 2010;**25**:159-164.

Chapter 6:
Sexual problems in elderly male and female patients with heart failure



Tialda Hoekstra, Ivonne Lesman-Leegte, Marie Louise Luttik, Robbert Sanderman, Dirk J. van Veldhuisen, Tiny Jaarsma

Heart 2012; Accepted for publication

Abstract

Objectives: To investigate perceived sexual problems in a large group of younger and older patients with heart failure (HF), with and without a partner, focusing on a broad range of perceived sexual problems, and compare this with a sample of healthy community dwelling elderly.

Design: Cross-sectional study.

Setting: 17 HF clinics and general practices in the Netherlands.

Participants: 438 Patients with HF and 459 healthy community-dwelling elderly

Main outcome measures: Differences in sexual functioning, related factors and perceived causes of sexual problems between patients with HF and healthy community controls.

Results: In total, 59% of HF patients reported sexual problems, mostly being problems with erectile function. HF patients with a partner (67%) and younger patients (65%) reported significantly more sexual problems than healthy community controls (resp. 58%, p=0.011 and 53%, p=0.011). Multivariate analyses show that sexual problems in HF patients with a partner were more common in men (OR 2.73, 95% CI 1.572 to 4.753) and in those with a prescription of beta-blockers (OR 2.00, 95% CI 1.10 to 3.586). In younger patients, sexual problems were independently associated with male gender (OR 3.21, 95% CI 2.099 to 4.908) and having a partner (OR 2.00, 95% CI 1.283 to 3.110). HF patients mainly attribute their sexual problems to symptoms of HF.

Conclusion: Sexual problems are common in patients with HF, particularly in younger patients and those with a partner. Since patients attribute their sexual problems mostly to heart failure symptoms, adequate treatment and education of HF patients is needed.

1. Introduction

Sexuality is a relevant component of quality of life, irrespective of a chronic condition such as heart failure (HF). Consequences of symptoms, treatment or psychological burden from being chronically ill or having a cardiac disease influences the quality of life of patients, and can affect sexual performance or cause sexual problems.[1] Symptoms of dyspnoea and fatigue may hinder the possibility of being active, and chest pain might cause patients to feel anxious during sexual activity.[2] Patients and their partners might fear deterioration as a result of sexual activity and death during intercourse.[3] Decreased frequency of sex, less satisfaction and loss of sexual interest were reported in HF patients at 3 and 9 months after a hospital admission.[4]

In earlier small studies sexual function of HF patients was studied in relatively young, married, and predominantly male patients, mainly addressing the prevalence of erectile dysfunction, and possibilities for treatment.[5-8] We recently reported that impaired sexuality is reported in approximately 50% of both male and female HF patients, as well as patients with and without a partner.[9] Considering the demographical characteristics of HF patients in daily practice, in which 50% is female and 30-50% are living alone,[10-12] more in-depth information is needed on the problems of both female and male patients, and patients with or without a partner.

At the same time it is known that there are age related changes in sexuality caused by normal hormonal changes, vascular damage, or muscular weakness that are independent of HF,[13] so it should be recognised that sexual problems might be part of the aging process, and not only be caused by HF. To contribute further to research on this subject, it is therefore important to have insight in the nature and cause of sexual problems of HF patients compared to healthy community-dwelling elderly people.

To get a clinically relevant perspective on the sexual problems of patients with HF, we aimed to study differences in sexual functioning, perceived causes, and related factors of sexual problems between HF patients and healthy community controls, both older and younger, and with and without a partner.

2. Methods

The present study has a descriptive cross-sectional design. The sample consisted of HF patients who completed the follow-up of the Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure (COACH) and a reference group of healthy community controls.[14,15]

2.1 Study population

2.1.1 Heart failure population

All patients were previously enrolled in the COACH study, a Dutch multicenter, randomized, controlled trial evaluating the effect of education and support in HF patients. Patients were included in the study during a hospitalisation for HF (New York Heart Association functional class II-IV), with HF as the primary diagnosis. Patients were followed during 18 months in which data on readmission and mortality were collected. During the last interview, 18 months after inclusion, 751 patients were alive and asked if they were willing to complete a questionnaire on sexual function at a later time point, and return it in a pre-stamped envelope. The Central Ethics Committee approved the study protocol and the amendment of the additional questionnaire on sexual function (METc 2002/047: Amendment 3). All patients provided informed consent. The study was performed in accordance with the principles outlined in the Declaration of Helsinki.[14,15]

2.1.2 Healthy community controls

Nine local district council offices in different areas in The Netherlands were asked for a random sample of addresses of 500-1000 subjects of at least 55 years of age who were not living at the same address. Between July and August 2005, 5500 questionnaires were distributed accompanied by a letter in which the subjects were invited to complete the questionnaire, and return it in a pre-stamped envelope. Anonymity and confidentially was guaranteed. Participants rated their health on a self-reported questionnaire on 19 active medical problems. From the 2512 elderly people, 1695 (67%) answered the questions on sexual function. Of these, 459 (27%) reported no health problems, and were selected for our comparison.

2.2 Study measures

2.2.1 Sexual problems

All participants were asked if they had problems with regard to interest, arousal, erection, vaginal dryness, orgasm or other problems. When answering affirmative to one or more of these questions they were considered as having sexual problems. Seven additional questions were added to describe the perceived cause of their sexual problems: shortness of breath, fatigue, pain, anxiety, anxiety of the partner, medication, and limited circulation. All additional questions were dichotomous with yes/no answer categories. The content, wording and validity of the questions were assessed by healthcare professionals, researchers and five patients with HF.

2.2.2 Importance and satisfaction with sex

All participants were asked to rate the importance and satisfaction with their sexual activity at this particular moment on a visual analogue scale ranging from 0 to 10 (0, very unimportant to 10, very important). Patients were also asked to rate the importance and satisfaction before their HF was diagnosed.

2.2.3 Sexual adjustment

Patients with HF completed the sexual adjustment subscale (SAS) of the psychosocial adjustment to illness scale.[16] This subscale has been used in previous studies in HF patients, describing shifts in the quality of sexual relations due to the current illness or treatment, and is composed of six items; change in sexual interest since illness, change in frequency of sexual activity, change in satisfaction, problems with sexual performance, arguments related to sex, problems with spouses. Each item has a scoring range of 0-3. For the SAS the total score ranges from 0 to 18. Low scores reflect good adjustment, whereas high scores indicate poor adjustment. The validity and reliability of the instrument has been established in a variety of clinical populations. The internal consistency of the subscales is acceptable with Cronbach alphas ranging from 0.74 to 0.80 in HF patients.[4,17] Due

to the orientation on adaptation to disease, the SAS was not administered to the community controls.

2.2.4 Demographic and clinical characteristics

Data on demographic and clinical characteristics were collected from chart review, interviews and questionnaires. Depressive symptoms were measured with the Center for Epidemiological Studies Depression scale (CES-D). A total sum score is used (0-60), with higher scores indicating more depressive symptoms.[18,19]

2.3 Statistical Analyses

Descriptive statistics were used to characterise both samples. For continuous variables means and standard deviations, and for categorical variables, frequencies with percentages were used. Differences on sexual problems, and importance and satisfaction with sexuality between community controls and patients with HF were tested by Chi^2 tests and an independent sample t-test. Importance and satisfaction with sexuality in patients with HF now and before HF was tested with a paired samples t-test.

Differences in demographic and clinical characteristics between patients with and without sexual problems were univariate tested with independent sample t-tests and Chi^2 tests. A multivariable logistic regression analysis was performed to define the independent association between sexual problems and demographic and clinical characteristics. The multivariate model was built by entering those variables that had a univariate $p<0.15$, and retaining those variables with $p<0.05$ in the final model. As previous studies showed that age and having a partner is associated with sexual problems, in order to gain more insight into sexual problems, we performed analyses independently for respondents of 65 years and younger and older than 65 years, and for respondents with or without a partner. The cut-off age of 65 years was decided on based on the mean age of both the patient and healthy community controls groups. Sixty-five years was about the median of the four values, and the value in which all groups still consisted of a considerable number of respondents for statistical analyses. Having a partner was

defined as 'married-living together', 'not married-living together', and 'having a partner-not living together'. Furthermore, in the total group the interaction between age and having a partner was included in the model.

3. Results

3.1 Patient characteristics

In total, 438 patients of the 751 HF patients (59%) returned completed questionnaires on sexual function. Patients who returned the questionnaires were slightly younger compared to those who did not return the questionnaires (68 (± 12) vs. 71 (± 11), p=0.001), were more often living with a partner (68% vs. 53%, p<0.001), and were more often in an intervention arm of the COACH study (care as usual 29% vs. 37%, basic intervention 34% vs. 33%, intensive intervention 38% vs. 31%, p=0.039). No differences were found with regard to gender.

Of the 438 patients 68% (298) had a partner. The mean age was 68 years (± 12), and 62% were men. Patients had a mean left ventricular ejection fraction of 33% (± 14), and were prescribed the standard HF medications; 74% of patients were prescribed a beta-blocker at the time of this study (Table 1).

Of the 459 healthy community controls, 87% (401) had a partner, with a mean age of 64 years (± 7), and 67% were men. In total, 13% of the healthy controls (n=58) did not have a partner, these had a mean age of 65 years (±8), and 55% were men.

Table 1. Patient characteristics[a]

	Total group (n=438)	With a partner (n=298)	Without a partner (n=140)	65 years and younger (n=155)	Older than 65 years (n=283)
Age, mean (SD), y	68 (12)	67 (12)	72 (13)*	55 (9)	76 (6)***
Male	270 (62)	216 (73)	54 (39)***	100 (65)	170 (60)
Intervention group					
Care as usual	125 (29)	81 (27)	44 (31)	38 (25)	87 (31)
Basic intervention	148 (34)	102 (34)	46 (33)	55 (35)	93 (33)
Intensive intervention	165 (38)	115 (39)	50 (36)	62 (40)	103 (36)
Length of relationship, mean (SD), y	38 (14)	38 (14)	-	27 (12)	45 (11)***
NYHA III-IV at 18 months	127 (32)	85 (31)	42 (33)	33 (23)	94 (36)*
LVEF, mean (SD) %	33 (14)	32 (14)	33 (14)	30 (14)	34 (14)*
Ischemic HF	168 (38)	123 (41)	45 (32)	38 (25)	130 (46)***
Stroke	37 (8)	22 (7)	15 (11)	5 (3)	32 (11)*
COPD	103 (24)	67 (23)	36 (26)	24 (16)	79 (28)*
Diabetes	94 (22)	63 (21)	31 (22)	33 (21)	61 (22)
ACE/ARB	354 (81)	242 (81)	112 (80)	133 (86)	221 (78)
Beta-blocker	305 (74)	218 (77)	87 (68)*	111 (77)	194 (73)
Diuretics[b]	384 (94)	266 (94)	118 (92)	130 (90)	254 (96)*
Lipid lowering drugs	187 (46)	134 (48)	53 (41)	61 (42)	126 (47)

Table 1. (Continued) Patient characteristics[a]

	Total group (n=438)	With a partner (n=298)	Without a partner (n=140)	65 years and younger (n=155)	Older than 65 years (n=283)
CES-D score, mean (SD)	11 (9)	11 (9)	11 (9)	11 (10)	11 (9)
With partner	298 (68)	-	-	116 (75)	182 (64)*
Older than 65 years	383 (65)	182 (61)	101 (72)*	-	-

* $p<0.05$ *** $p<0.001$

[a] Data are presented as No. (%) of participants unless otherwise indicated

[b] Loopdiuretics, thiazides and aldostorone-antagonists

Abbreviations: NYHA=New York Heart Association functional class; LVEF=Left Ventricular Ejection Fraction; COPD=Chronic Obstructive Pulmonary Disease; ACE/ARB=Angiotensin Converting Enzyme Inhibitor or Angiotensin Receptor Blocker; CES-D=Center for Epidemiological Studies Depression Scale.

Table 2. Problems and attributed causes in HF patients and community controls[a]

	Total group (n=897)		With a partner (n=699)		Without a partner (n=198)		65 years and younger (n=453[b])		Older than 65 years (n=439[b])	
	CC (n=459)	HF (n=438)	CC (n=401)	HF (n=298)	CC (n=58)	HF (n=140)	CC (n=298)	HF (n=155)	CC (n=156)	HF (n=283)
Problems in sexual function	259 (56)	259 (59)	231 (58)*	200 (67)	28 (48)	59 (42)	157 (53)*	101 (65)	99 (64)	158 (56)
No interest in sex	53 (12)	56 (13)	47 (12)	40 (13)	6 (10)	16 (11)	28 (9)	19 (12)	23 (15)	37 (13)
No sexual arousal	47 (10)	50 (11)	41 (10)	38 (13)	6 (10)	12 (9)	29 (10)	21 (14)	18 (12)	29 (10)
Problems with erection (males)	52 (17)***	101 (37)	46 (17)***	83 (38)	6 (19)	18 (33)	19 (10)***	39 (39)	33 (30)	62 (37)
Problems with vaginal lubrication (females)	50 (31)***	10 (6)	45 (34)***	10 (12)	5 (19)***	0 (0)	36 (33)*	5 (9)	14 (30)***	5 (4)
Problems with orgasm	36 (8)	41 (9)	35 (9)	34 (11)	1 (2)	7 (5)	16 (5)	14 (9)	19 (12)	27 (10)
Other problems	57 (12)	42 (10)	50 (13)	28 (9)	7 (12)	14 (10)	44 (15)	20 (13)	13 (8)	22 (8)

Table 2. (Continued) Problems and attributed causes in HF patients and community controls[a]

	Total group (n=897)		With a partner (n=699)		Without a partner (n=198)		65 years and younger (n=453[b])		Older than 65 years (n=439[b])	
	CC (n=459)	HF (n=438)	CC (n=401)	HF (n=298)	CC (n=58)	HF (n=140)	CC (n=298)	HF (n=155)	CC (n=156)	HF (n=283)
Causes of changes in sexual function										
Shortness of breath	2 (0)*	86 (20)	2 (1)***	68 (23)	0 (0)*	18 (13)	1 (0)***	32 (21)	1 (1)***	54 (19)
Fatigue	37 (8)***	87 (20)	35 (9)***	75 (25)	2 (3)	12 (9)	22 (7)***	44 (28)	15 (10)	43 (15)
Pain	20 (4)	13 (3)	18 (5)	10 (3)	2 (3)	3 (2)	12 (4)	5 (3)	8 (5)	8 (3)
My anxiety	21 (5)	26 (6)	18 (5)	22 (7)	3 (5)	4 (3)	8 (3)*	16 (10)	13 (8)*	10 (4)
Anxiety of my partner	23 (5)	13 (3)	23 (6)	13 (4)	-	-	13 (4)	6 (4)	11 (7)*	7 (3)
Medication	9 (2)***	43 (10)	8 (2)***	37 (12)	1 (2)	6 (4)	3 (1)***	22 (14)	6 (4)	21 (7)
Limited circulation	26 (6)*	48 (11)	24 (6)**	42 (14)	2 (3)	6 (4)	16 (5)*	18 (12)	10 (6)	30 (11)

[a] Data are presented as No. (%) of participants

[b] Missing data on age of 5 community controls

*p <0.05 ***p<0.001

Abbreviations: CC=Community Controls; HF=Heart Failure patients

3.2 Sexual problems

In total, 59% of the patients reported problems with sexual function, compared to 56% of the healthy community controls (Table 2). Patients reporting sexual problems were younger (67 vs. 70 years, p=0.025), were more often men (75% vs. 43%, p<0.001), were diagnosed with ischemic HF (44% vs. 31%, p=0.006), had a partner (77% vs. 55%, p<0.001), and had more often a prescription of beta-blockers (80% vs. 66%, p=0.002), and lipid-lowering drugs (51% vs. 37%, p=0.007). In multivariate analyses, variables that were independently related to reporting sexual problems were male gender, a prescription of beta-blockers, and having a partner. The interaction of age and having a partner was not significant related to reporting problems (Table 3).

3.3 Sexual problems in younger and older respondents

Patients who were 65 years and younger reported significantly more sexual problems compared to healthy controls of the same age category, this was not found in patients older than 65 years compared to healthy controls. Younger male patients reported more often problems with erectile function than the healthy controls. However, in both the younger and older respondents female patients reported less often problems with vaginal lubrication than female controls (Table 2).

Independent of age category, patients rated the importance and their current satisfaction of sexuality lower than before their disease, and lower than healthy community controls. All patients did perceive sexuality as less important, and were less satisfied with their current sexuality than before their HF (Figure 1).

Younger patients had a mean total score of 6.0, and older patients of 7.5 on the SAS, with higher scores reflecting more perceived problems. Most problems, both in younger and older patients, were found on the items related to the change in frequency of sexual activity, and the least problems on describing arguments with their spouses related to their sexual relationship. Shortness of breath and anxiety were reported more often as the cause of sexual problems in both younger and older patients compared to healthy controls. Younger patients also reported

fatigue, medication, and limited circulation more often to be the cause of their problems, unlike the older patients, who reported more often their partners' anxiety to be the cause of their problems compared to the healthy community controls of the same age category (Table 2).

Different associations were found between sexual problems in younger and older patients. In younger patients male gender, and having a partner were independently associated with problems in sexual functioning. In older patients male gender and a prescription of beta-blockers were independently associated with sexual problems (Table 3).

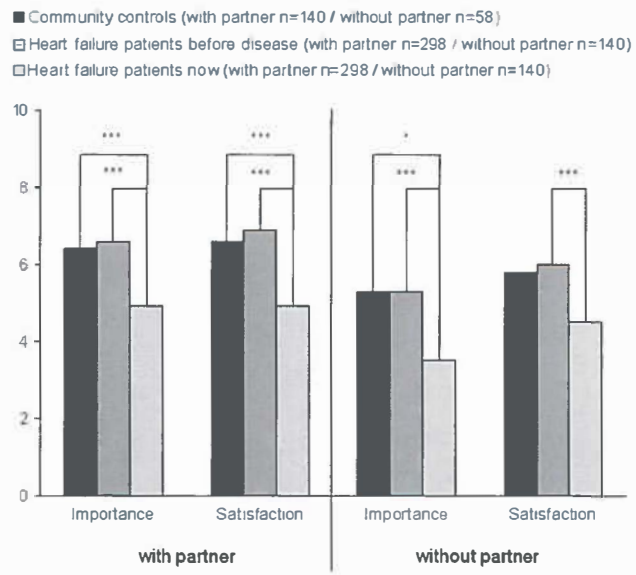
3.4 Sexual problems in respondents with and without partner

Patients with a partner significantly more often perceived sexual problems compared to healthy controls. Patients without a partner did not report more sexual problems than the healthy controls without a partner. In respondents with a partner, male patients reported significantly more problems with erectile function than healthy controls (Table 2).

Patients had a mean total score on the SAS of 6.8. No differences were found between patients with or without a partner. Shortness of breath was more often reported as cause of sexual problems in patients than healthy controls, independent of having a partner (Table 2).

Different associations were found between sexual problems in patients with or without partner. In patients with a partner male gender and a prescription of beta-blockers were independently associated with problems in sexual functioning. In patients without a partner male gender, ischaemic HF, a prescription of beta-blockers, and a higher score on the CES-D were independently associated with sexual problems (Table 3).

A



B

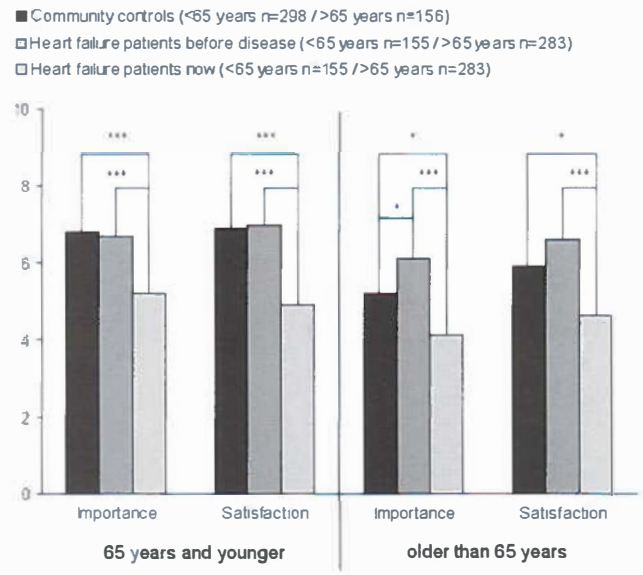


Figure 1. Importance and satisfaction with sexual activity of community controls and heart failure patients. *p<0.05, ***p<0.001.

A. Respondents with and without a partner.

B. Respondents younger and older than 65 years.

Table 3. Multivariate analyses problems in sexual function of HF patients

	B (SE)	Odds Ratio (95% CI)	p-value
Total group (n=438)			
Male	1.4 (0.2)	3.93 (2.50 to 6.18)	<.001
Beta-blocker at 18 months	0.7 (0.3)	2.05 (1.26 to 3.33)	.004
Having a partner	0.6 (0.2)	1.73 (1.08 to 2.78)	.02
Patients with a partner (n=298)			
Male	1.0 (0.3)	2.73 (1.57 to 4.75)	<.001
Beta-blocker at 18 months	0.7 (0.3)	1.99 (1.10 to 3.59)	.02
Patients without a partner (n=140)			
Male	2.0 (0.5)	7.37 (3.05 to 17.79)	<.001
Ischemic HF	1.4 (0.5)	3.99 (1.54 to 10.34)	.004
Beta-blocker at 18 months	1.1 (0.03)	3.12 (1.18 to 8.24)	.02
CES-D score	-2.9 (0.7)	1.05 (1.00 to 1.11)	.04
Patients ≤ 65 years (n=155)			
Male	1.2 (0.2)	3.21 (2.10 to 4.91)	<.001
Having a partner	0.7 (0.2)	2.00 (1.28 to 3.11)	.002
Patients > 65 years (n=283)			
Male	1.6 (0.3)	5.18 (3.00 to 8.96)	<.001
Beta-blocker at 18 months	1.0 (0.3)	2.60 (1.43 to 4.73)	.002

4. Discussion

Our results show that sexual problems are common in patients with HF. Considering these problems in the total population of patients, without taking age or marital status into account; these problems are comparable with healthy community controls. However, when looking specifically to participants with and without a partner, and older and younger participants, HF patients with a partner and younger patients reported a significant reduction in their satisfaction with sexuality, and perceived more sexual problems compared to healthy community controls. In younger patients male gender and having a partner were independently associated with problems in sexual functioning. In patients with a partner male gender and having a prescription for beta-blockers were associated with sexual problems. Based on previous studies, we expected more reported sexual problems in the HF population. This was not the case. A possible explanation could be that these studies predominantly focused on younger male patients and patients with a partner.[5-8] Our total study sample also included older female patients, and patients without a partner. Our results show that a large percentage of these patients do report sexual problems; however, it did not differ significantly from the healthy community controls.

This is the first study with a considerable patient sample that examined specific and in-depth sexual problems in HF patients compared to healthy community controls. It is known that changes in sexuality might be part of the aging process (hormonal changes, vascular damage, or muscular weakness) and are not only caused by HF.[13] In order to gain more insight into age-related sexual problems, we chose to analyse data separately for respondents older and younger than 65 years. Our study is also unique in the sense that we chose to include male and female patients, and patients both with and without a partner. Of course, we realize that having a partner is strongly associated with the perception of sexual problems, as patients who have a partner can be expected to be confronted more often with those problems as part of their daily life.[20] Therefore, we analysed participants with and without a partner separately.

Patients and their partners might worry about sexual problems. Our study confirmed previous reports of the higher prevalence of erection problems in cardiac patients compared to a non-cardiac population.[21] A decreased frequency and decreased interest were reported by patients as result of their HF. Although more male patients perceive sexual problems, we also found a large number of women (25% of the total group) reporting sexual problems, suggesting that the main focus on men in research regarding sexual problems in cardiovascular disease does not seem appropriate.[22] In general, HF symptoms like dyspnoea, fatigue, and exercise intolerance can be assumed to affect sexuality in both male and female patients. This seems to be confirmed by our results, which show that all patients attribute their sexual problems to their HF symptoms, and therefore it is important to address the possible influence of HF and HF-medication in patient education and treatment. In particular, the attribution of sexual problems to medication can lead to non-compliance with the treatment regimen. In our study female patients also reported problems with arousal, interest, and orgasms. Only a minority of the female patients reported problems with vaginal lubrication, which was significantly less often reported compared to healthy controls.

We found an independent relationship between prescriptions of beta-blockers and sexual problems in patients with and without a partner, and also in older patients. Until now results from studies addressing the relationship between beta-blocker use and sexual problems are incongruent.[23,24] Animal studies have reported that beta-blockers such as propanolol may induce erectile dysfunction through central and peripheral (genital) effects as it increases the latency to ex copula ejaculation, the latency to initial erection, and reduces the number of erectile reflexes.[25] However, Silvestri et al. suggest that reports of erectile dysfunction in patients receiving beta-blockers may be mostly psychological in origin as it is more frequent in patients knowing the side effect of the drug, and it is reversed in the majority of cases by placebo.[24]

Despite earlier hypothesising about the possible anxiety of patients affecting the return to sexual activity, only 6% of the HF patients described their own anxiety, and 3% the anxiety of their partner as a reason for sexual problems.[2] Depressive

symptoms are known to be related to sexual problems,[26,27] and we found that patients with sexual problems had higher CES-D scores, and depressive symptoms were independently related to sexual problems in patients without a partner.

Furthermore, it is interesting to note that HF patients rated the importance and satisfaction with their current sexuality significantly lower than before their disease. Looking back on their sex life before their HF the importance and satisfaction with sexuality was the same as the community controls. However, patients perceive sexuality as less important, and were less satisfied with current sexuality (eg, having diagnosed HF) than community controls. This possibly reflects adaption of priorities and expectations in life when living with a chronic disease.[28]

Several limitations of this study should be considered. First, the list of characteristics of the community controls was limited, and only included age, gender, having a partner and the presence of medical problems. Given the age group, a high percentage of morbidity would be expected, with sexual problems as a possible consequence. Therefore, in order to make a representative comparison, community controls who reported health problems were excluded from our analyses. A second limitation of this study is the response of the survey, which was 59%. Although this is an acceptable response, and comparable to other surveys, this needs to be taken into account because it is reasonable that patients with problems were more motivated to return the questionnaires. On the contrary, it can be imagined that patients have some reluctance in reporting sexual problems, even in an anonymous survey. Several studies on the accuracy of self reports of sexual behaviour have shown that a survey design provides lower reports of sensitive behaviours compared to several different interview techniques.[29,30] Therefore, it is also reasonable to suggest that the number of patients actually having problems with sexual functioning is higher than the number of patients who report having problems.

4.1 Implications for clinical practice

Patients with HF, both male and female, with a partner and younger patients experience more sexual problems than healthy community-dwelling elderly people. However, also a large percentage of older patients and patients without a partner also report sexual problems, and all patients attribute these problems to HF-related symptoms. These findings emphasise that sexual health needs to be discussed with all patients with HF during treatment, and should become an integral part of HF management and patient education. Healthcare providers should create an environment where patients feel comfortable enough to talk about their concerns, in the confidence that these will be addressed.

4.2 Implications for further research

Sexual problems in patients with HF are more often reported than to be expected as part of the aging process. Further research is needed on interventions to improve sexual activity, including sexual counselling. These studies should not only address younger and male patients, but also include female and older patients. Furthermore, future research on pharmacological and non-pharmacological interventions should include sexual activity and sexual function, in order to gain more insight into the effects of the treatment on sexual health.

5. Conclusions

Patients with HF with a partner and younger patients experience significantly more sexual problems than healthy community controls. In addition, a large percentage of older patients and patients without a partner report having sexual problems, and all patients attribute these to HF-related symptoms. Therefore, healthcare providers need to discuss the possible consequences of HF, HF symptoms and HF medications on sexual health with their patients on a regular basis, in order to help patients cope with their sexual problems.

References

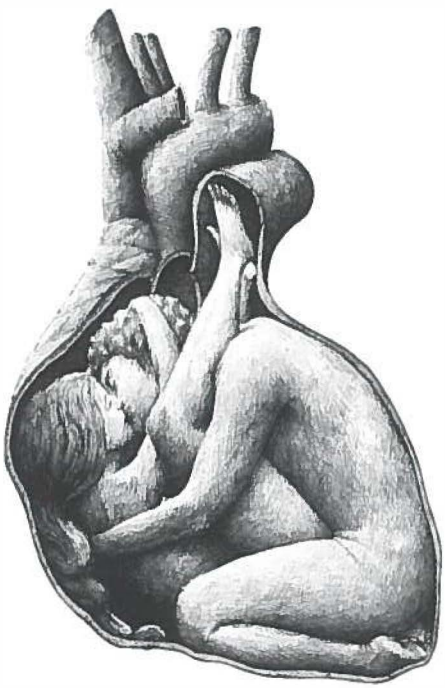
1. Hoekstra T, Lesman-Leegte I, van Veldhuisen DJ, Sanderman R, Jaarsma T. Quality of life is impaired similarly in heart failure patients with preserved and reduced ejection fraction. *Eur J Heart Fail* 2011;**13**:1013-1018.
2. Steinke EE, Wright DW, Chung ML, Moser DK. Sexual self-concept, anxiety, and self-efficacy predict sexual activity in heart failure and healthy elders. *Heart Lung* 2008; **37:**323-333.
3. Schwarz ER, Kapur V, Bionat S, Rastogi S, Gupta R, Rosanio S. The prevalence and clinical relevance of sexual dysfunction in women and men with chronic heart failure. *Int J Impot Res* 2008;**20**:85-91.
4. Jaarsma T. Sexual problems in heart failure patients. *Eur J Cardiovasc Nurs* 2002;**1**:61-67.
5. Jaarsma T, Dracup K, Walden J, Stevenson LW. Sexual function in patients with advanced heart failure. *Heart Lung* 1996;**25**:262-270.
6. Steinke EE, Mosack V, Wright DW, Chung ML, Moser DK. Risk factors as predictors of sexual activity in heart failure. *Dimens Crit Care Nurs* 2009;**28**:123-129.
7. Rastogi S, Rodriguez JJ, Kapur V, Schwarz ER. Why do patients with heart failure suffer from erectile dysfunction? A critical review and suggestions on how to approach this problem. *Int J Impot Res* 2005;**17**(Suppl 1):S25-S36.
8. Schwarz ER, Rastogi S, Kapur V, Sulemanjee N, Rodriguez JJ. Erectile dysfunction in heart failure patients. *J Am Coll Cardiol* 2006;**48**:1111-1119.
9. Hoekstra T, Jaarsma T, Sanderman R, van Veldhuisen DJ, Lesman-Leegte I. Perceived sexual dysfunction and associated factors in patients with heart failure. *Am Heart J* 2012;**163**:246-251.
10. Cleland JG, Swedberg K, Follath F, et al. The EuroHeart Failure survey programme--a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis. *Eur Heart J* 2003;**24**:442-63.

11. Heo S, Moser DK, Chung ML, Lennie TA. Social status, health-related quality of life, and event-free survival in patients with heart failure. *Eur J Cardiovasc Nurs* 2012;**11**:141-149.
12. Gallagher R, Luttik ML, Jaarsma T. Social support and self-care in heart failure. *J Cardiovasc Nurs* 2011;**26**:439-445.
13. Wylie K, Kenney G. Sexual dysfunction and the ageing male. *Maturitas* 2010;**65**:23-27.
14. Jaarsma T, Van Der Wal MH, Hogenhuis J, et al. Design and methodology of the COACH study: a multicenter randomised Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure. *Eur J Heart Fail* 2004;**6**:227-233.
15. Jaarsma T, van der Wal MH, Lesman-Leegte I, et al. Effect of moderate or intensive disease management program on outcome in patients with heart failure: Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH). *Arch Intern Med* 2008;**168**:316-324.
16. Derogatis L. *Scoring and procedures manual for PAIS*. Baltimore, MD: Clinical Psychometric Research; 1976.
17. Westlake C, Dracup K, Walden JA, Fonarow G. Sexuality of patients with advanced heart failure and their spouses or partners. *J Heart Lung Transplant* 1999;**18**:1133-1138.
18. Radloff L. The CES-D scale. A self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;**1**:385-401.
19. Jaarsma T, Lesman-Leegte I, Hillege HL, Veeger NJ, Sanderman R, van Veldhuisen DJ. Depression and the usefulness of a disease management program in heart failure: insights from the COACH (Coordinating study evaluating Outcomes of Advising and Counseling in Heart failure) study. *J Am Coll Cardiol* 2010;**55**:1837-1843.
20. Dalteg T, Benzein E, Fridlund B, Malm D. Cardiac disease and its consequences on the partner relationship: A systematic review. *Eur J Cardiovasc Nurs* 2011;**10**:140-149.

21. Russell ST, Khandheria BK, Nehra A. Erectile dysfunction and cardiovascular disease. *Mayo Clin Proc* 2004;**79**:782-794.
22. Steinke EE. Sexual dysfunction in women with cardiovascular disease: what do we know? *J Cardiovasc Nurs* 2010;**25**:151-158.
23. Rosen RC, Kostis JB, Jekelis A, Taska LS. Sexual sequelae of antihypertensive drugs: treatment effects on self-report and physiological measures in middle-aged male hypertensives. *Arch Sex Behav* 1994;**23**:135-152.
24. Silvestri A, Galetta P, Cerquetani E, et al. Report of erectile dysfunction after therapy with beta-blockers is related to patient knowledge of side effects and is reversed by placebo. *Eur Heart J* 2003;**24**:1928-1932.
25. Srilatha B, Adaikan PG, Arulkumaran S, Ng SC. Sexual dysfunction related to antihypertensive agents: results from the animal model. *Int J Impot Res* 1999;**11**:107-113.
26. Mosack V, Steinke EE, Wright DW, et al. Effects of depression on sexual activity and sexual satisfaction in heart failure. *Dimens Crit Care Nurs* 2011;**30**:218-225.
27. Levine GN, Steinke EE, Bakaeen FG, et al. Sexual activity and cardiovascular disease: A scientific statement from the American Heart Association. *Circulation* 2012;**125**:1058-1072.
28. Verschuren JE, Enzlin P, Dijkstra PU, Geertzen JH, Dekker R. Chronic disease and sexuality: a generic conceptual framework. *J Sex Res* 2010;**47**:153-170.
29. Plummer ML, Ross DA, Wight D, et al. "A bit more truthful": the validity of adolescent sexual behaviour data collected in rural northern Tanzania using five methods. *Sex Transm Infect* 2004;**80**:ii49-56.
30. Langhaug LF, Chueng YB, Pascoe, et al. How you ask really matters: randomised comparison of four sexual behaviour questionnaire delivery modes in Zimbabwean youth. *Sex Transm Infect* 2011;**87**:165-173.

Chapter 7:

What keeps nurses from the sexual counseling of patients with heart failure?



Tialda Hoekstra, Ivonne Lesman-Leegte, Margriet F. Couperus, Robbert Sanderman, Tiny Jaarsma

Heart & Lung 2012;41:492-499

Abstract

Objectives: We sought to examine the current practice of discussing sexual health by heart failure (HF) nurses, and to explore which barriers prevent nurses from discussing sexuality.

Methods: The Nurses' Survey of Sexual Counseling of Myocardial Infarction Patients and a list of berriers were used to form a questionnaire, which was sent to all HF clinics (n=122) in The Netherlands.

Results: The majority (75%) of nurses (n=146) felt a certain responsibility to discuss patients' sexual health. However, in practice, 61% of the nurses rarely or never addresses sexuality. Barriers that prevented nurses from addressing sexuality and that differed between nurses who do (n=58) and do not (n=88) discuss sexuality include a lack of organizational policy (49% vs. 79%, respectively; $p<0.001$), lack of training (43% vs. 80%, respectively; $p<0.001$), and not knowing how to initiate the subject (24% vs. 72%, respectively; $p<0.001$). Nurses preferred to address sexuality during a follow-up visit or when discussing medication.

Conclusions: Although HF nurses feel responsible for discussing sexuality, this topic is rarely addressed in clinics. Several barriers were identified, relating to personal, patient, and organizational factors.

1. Introduction

Sexual problems are common among both male and female patients with heart failure (HF).[1,2] Problems reported by patients with HF include a decrease in sexual interest, a decrease in the frequency of sexual activity, severe negative changes in sexual performance, and a loss of pleasure or satisfaction related to sexual activity. Furthermore, a significant proportion of men with HF experience erectile dysfunction.[1-3] Patients attribute their sexual problems to their HF. In addition, HF medications may also lead to sexual problems. The use of beta-blockers in particular is known to exert a possible detrimental effect on sexuality, although studies addressing the relationship between beta-blockers and sexual problems have been incongruent.[4,5]

Patients with HF and their partners have expressed a wish to receive information about resuming sexual activity after a diagnosis of HF.[6] However, when trying to address this topic, patients experience barriers, such as the perception that individual practitioners do not appear experienced enough to understand the patient's problems, or because feelings of shyness and embarrassment prevent them from initiating discussions.[7] In this respect, nurses play an important role in assessing the effects of HF on sexuality with both patients and their partners. This becomes even more apparent when taking into account the fact that HF nurses are becoming more and more involved in the long-term management of patients with HF.

Although international HF guidelines recommend that healthcare providers discuss sexual health with their patients, previous studies showed that although healthcare providers do feel responsible for discussing sexual health, they rarely discuss this topic with their patients in practice.[8-11] To improve patient care in this area, it is important to learn which barriers prevent nurses from discussing sexual health with their patients. A study of cardiac rehabilitation staff showed that barriers included lack of training, the feeling that the patient was not yet ready to discuss issues related to sexual health, and a general lack of knowledge concerning sexual health.[11]

Unfortunately, little information is available on the current practice of discussing sexual health and providing sexual counselling by HF nurses in The Netherlands. Therefore, this study was designed to examine: (1) the current practice of discussing

sexual health in HF clinics in The Netherlands and the perceived responsibility of nurses to address patients' sexual health; (2) the preferred moment during HF treatment to address patients' sexual concerns; and (3) differences in barriers to sexual counselling between nurses who do and who do not discuss this topic.

2. Methods

2.1 Study participants

A letter of introduction was sent to all HF clinics in the Netherlands (n=122), which included 3 copies of a questionnaire and a freepost return envelope.[12,13] We included three copies because, in general, a maximum of 3 HF nurses works at each HF clinic. In the letter of introduction, nurses working at the specific HF clinic were asked to complete the (anonymous) questionnaire and return it within 2 weeks. Non-responders received a reminder in the form of a telephone call after 3 weeks. Confidentiality was guaranteed to the participants of the study, and answers could not be traced back to individual nurses.

2.2 Questionnaire

Two questionnaires used in previous studies formed the basis of the current questionnaire. These included 2 subscales of the Nurses' Survey of Sexual Counseling of Myocardial Patients, and a list of barriers used by Doherty et al.[11,14,15]

(1) The subscales for practice and responsibility of the Nurses' Survey of Sexual Counseling of MI patients were used in this study: The subscale "Practice" (8 items) addresses the overall practice of sexual counseling. For example, "In the past year, with what percentage of your clients have you assessed their sexual health?" Four items were scored on a scale of 0 to 3, and 4 items were scored on a scale of 0 to 5. The subscale scores ranged from 0 to 32, with higher scores indicating better performance of nurses on sexual counseling in daily practice. To clarify the data, the scores on the 6 answer categories were translated into "never"

(0%), "sometimes" (1-20% and 21-40%), and "often" (41-60%, 61-80%, and 81-100%).

The subscale "Responsibility" (5 items) addresses the perceived responsibility of nurses to provide sexual counseling. For example, "Nurses have a responsibility to discuss sexual health with their patients" (responses range from "strongly agree" to "strongly disagree"). All items were scored on a scale from 0 to 4. The subscale scores ranged from 0 to 20, with higher scores indicating a greater sense of responsibility to provide sexual counseling. Reliability of the subscales was assessed using Cronbach's alpha and ranged from 0.89 (practice) to 0.75 (responsibility).[14]

(2) The list of barriers that prevent nurses from discussing sexual health consisted of 16 items, as devised by Doherty et al.[11] To gain further insights into other possible barriers, 8 additional items on barriers were retrieved from discussions among a group of experts (including a cardiologist, a sexologist, HF nurses, and psychologists) and added to the list. These included: lack of organizational policy (eg, is a protocol on sexual health available?), lack of knowledge on how to initiate the subject, the patient's failure to initiate the subject, sexuality as a private matter, no feeling of connection with the patient, discomfort in addressing the topic, projecting personal feelings on the patient (eg, "I would find it unpleasant myself"), and the patient is of the same sex. Scores on each item could range from 1 ("strongly disagree") to 5 ("strongly agree").

In addition, participants had to answer 10 questions on sociodemographics and on their professional background. The face validity of the total questionnaire was tested in a pilot study by 4 HF nurses. Only editorial changes were effected in response to the nurses' answers.

2.3 Statistical analyses

Data were analyzed using SPSS, version 16.0 (SPSS Inc, Chicago, IL). Descriptive analyses were used to test the sample and the responses to the study variables.

Data are presented as means ± standard deviations or percents. We used Chi² tests to compare the perceived barriers of nurses who do discuss sexual health with the barriers of nurses who do not discuss sexuality with their patients. A p-value of <0.05 was considered statistically significant. For comparing the barriers of nurses who do and who do not discuss sexual health, the scores on the barriers were recoded to agree ("strongly agree" and "agree") and disagree ("strongly disagree" and "disagree"). The answer category "somewhat (dis)agree" was not included in the analyses. Scores on discussing sexual health were based on answers to the first question of the practice subscale: "How often is sexual health assessed in your practice?" The scores were recoded into do discuss ("often" and "occasionally") and do not discuss ("rarely" and "never").

3. Results

3.1 Study population

In total, nurses from 88 of the 122 (72%) HF clinics responded by returning at least 1 completed questionnaire. The final sample of respondents consisted of 146 nurses. The majority of nurses was female (83%), with a mean age of 45 (± 8) years (age range 25-61 years). In total, 67% of nurses had a Bachelor's degree, and 30% reported going on to higher education or workshops on sexuality in nursing practice (Table 1).

Table 1. Nurse characteristics

	Total (n=146)	Nurses who do discuss sexuality (n=58)	Nurses who do not discuss sexuality (n=88)	p-value
Female gender	83%	81%	88%	.236
Age	45 ± 8	45 ± 8	46 ± 7	.830
Marital status				
Married/living with a partner	88%	88%	87%	
Never married	9%	12%	7%	.353
Divorced/widowed	3%	0%	6%	
Years in cardiac nursing				
0-5 years	32%	31%	32%	
6-10 years	32%	38%	28%	.422
>10 years	36%	31%	40%	
Highest level of education				
Basic nursing training	14%	10%	17%	
Bachelor degree	67%	69%	67%	.654
Master degree	5%	5%	5%	
Other	14%	16%	11%	
Education in sexual counseling	30%	41%	22%	.012

3.2 Practice and responsibility

The subscale "Practice" had a mean score of 10 (± 4) (range, 2 to 24; higher scores indicate a better performance of nurses for discussing sexual health in daily practice). When looking at specific items, 1% of nurses reported that they frequently assessed sexual health with their patients, 38% did so occasionally, 53% did so rarely, and 8% never assessed sexual health with their patients. Furthermore, 50% of nurses never referred patients with questions about sexuality to other professions (Figure 1), whereas 49 % sometimes did so.

The subscale "Responsibility" yielded a mean score of 15 (± 2) (range, 7 to 20, higher scores indicate a greater sense of responsibility among nurses to initiate sexual counseling). In total, 75% of nurses agreed that they have a responsibility to discuss sexual health with their clients; whereas 11% disagreed, and 14% were not sure. Moreover, 37% reported that initiating a discussion on sexual health with patients is usually appropriate, whereas 5% of nurses stated that initiating such a discussion is always inappropriate (Figure 2).

No significant differences in background variables were evident between nurses who do and nurses who do not discuss sexual health with their patients. However, significantly more nurses who do discuss sexual health had received education on sexual counseling, compared with nurses who do not discuss sexual health (41% vs. 22%, respectively; p=0.012) (Table 1).

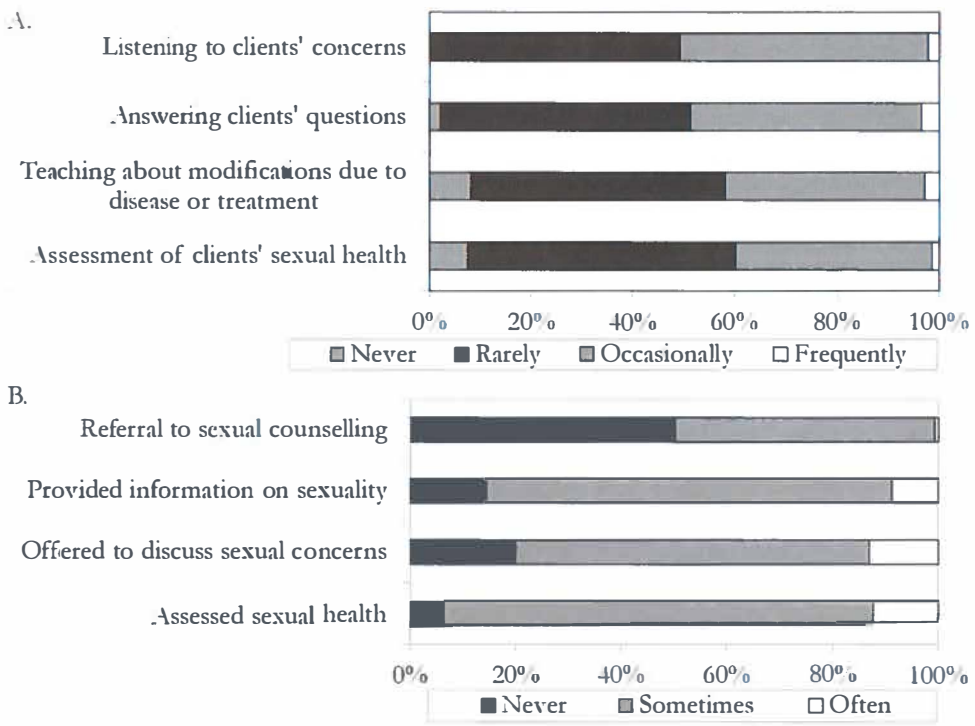


Figure 1. Practice of discussing sexual health by HF nurses.

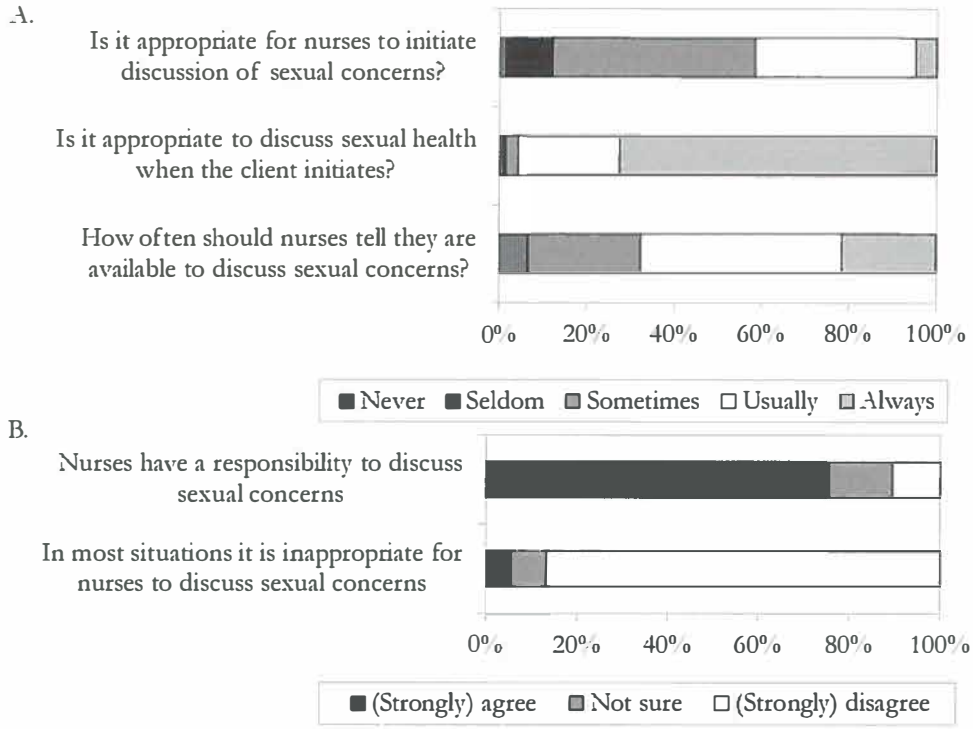


Figure 2. Perceived responsibility of HF nurses to discuss sexual health.

3.3 Preferred moment of discussing sexual health

The majority of nurses (74%) agreed that sexual health should be assessed during a follow-up visit at the HF clinic or when discussing medication with the patient (72%). Thirty percent of nurses felt that sexual health should be discussed during the first visit to the HF clinic, 34% preferred to discuss sexual health during cardiac rehabilitation, and 13% preferred to address this topic during hospital admission (Figure 3).

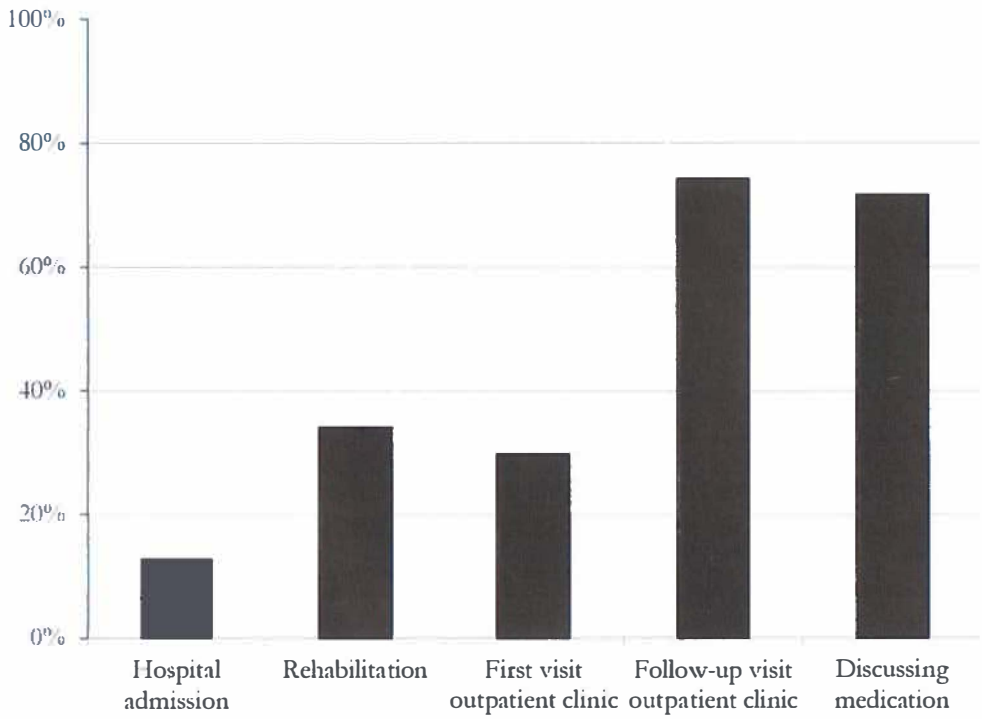


Figure 3. Preferred moment of discussing sexual health.

3.4 Barriers to discussing sexual health

The most prominent barriers that deterred nurses from discussing sexual health with their patients included a lack of organizational policy (67%), a lack of training (42%), issues relating to culture and religion (40%), and the age of the patient (39%). Barriers mentioned in the questionnaire that did not keep nurses from discussing sexual health included: (1) they do not perceive counseling to be their task (3%), (2) the patient is of the same sex (0%), and (3) the patient is of the opposite sex (1%).

We looked in more detail at the differences in barriers between nurses who reported that they do discuss ("often" and "occasionally") sexual health with their

patients (n=58) and those who do not discuss' ("rarely" and "never") this topic (n=88).

Nurses who reported discussing sexual health with their patients mentioned several barriers to addressing this topic: issues related to culture and religion (68%), issues related to language and ethnicity (56%), patients too ill to address their sexual health (54%), sexuality not seen as a problem by the patient (53%), and a lack of organizational policy (49%). Nurses who rarely or never address sexual health mentioned several barriers: a lack of organizational policy (79%), a lack of training (80%), failure of the patient to initiate the subject (72%), a lack of knowledge on how to initiate the subject (71%), the older age of the patient (60%), and a lack of knowledge on the topic in general (57%).

Barriers that differed significantly between nurses who do and who do not discuss sexual health with their patients included a lack of knowledge (57% vs. 23%, respectively; $p=0.001$), a lack of training (80% vs. 43%, respectively; $p<0.001$), not knowing how to initiate the subject (71% vs. 32%, respectively; $p=0.001$), "I would find it unpleasant myself" (18% vs. 2%, $p=0.015$), "It makes me feel uncomfortable" (20% vs. 5%, respectively; $p= 0.036$), failure of the patient to initiate the subject (72% vs. 24%, respectively; $p<0.001$), and a lack of organizational policy (79% vs. 49%, respectively; $p<0.001$) (Table 2).

Table 2. Barriers withholding nurses who do and do not discuss sexual health with their patients

Barrier	Total group (n=146)	Nurses who do discuss sexuality (n=58)	Nurses who do not discuss sexuality (n=88)	p-value
Lack of organizational policy	67%	49%	79%	<.001
Lack of training	42%	43%	80%	<.001
Issues relating to culture and religion	40%	68%	53%	.121
Older aged patient	39%	43%	60%	.084
Issues relating to language and ethnicity	38%	56%	54%	.832
Not knowing how to initiate the subject	35%	32%	71%	<.001
Patient does not initiate the subject	35%	24%	72%	<.001
Patient is too ill to address sexual issues	35%	54%	45%	.395
Lack of knowledge	28%	23%	57%	.001
Sexuality is not seen as a problem for the patient	22%	53%	33%	.074
Sexuality is private	19%	23%	33%	.253
Concerns about increasing patients anxiety and discomfort	19%	17%	33%	.078
Patients lack of readiness	19%	45%	32%	.225
Presence of a third party	18%	23%	24%	.906
Not enough time	13%	19%	12%	.275
Embarrassment	10%	14%	16%	.837

Table 2. (Continued) Barriers withholding nurses who do and do not discuss sexual health with their patients

Barrier	Total group (n=146)	Nurses who do discuss sexuality (n=58)	Nurses who do not discuss sexuality (n=88)	p-value
Feeling no connection with the patient	10%	11%	15%	.561
It makes me uncomfortable	9%	5%	20%	.036
I would find it unpleasant myself	8%	2%	18%	.015
Fear of offending the patient	8%	11%	12%	.979
Too large an age difference between you and the patient	6%	2%	11%	.071
Someone else's job	3%	0%	6%	.075
Patient is of the opposite sex	1%	0%	1%	.400
Patient is of the same sex	0%	0%	0%	-

4. Discussion

To the best of our knowledge, this is the first study of HF nurses that explores the preferred moment of discussing sexual health and providing sexual counseling, and that examines differences in barriers between those nurses who do and who do not assess sexual health with their patients.

Our findings suggest that the majority of HF nurses (61%) do not assess sexual health, although the HF nurses (74%) in our study do feel responsible for discussing sexual health with their patients and offering them sexual counseling. This finding is comparable with those in other studies that looked at the feelings of responsibility experienced by cardiac healthcare providers and the practices regarding sexual counseling in cardiac settings. In a European survey on the practice and responsibility of nurses to provide sexual counseling to cardiac patients, 87% of the cardiac nurses agreed that nurses have a responsibility to discuss sexual health. However, only 11% of the nurses discussed the subject frequently with their patients.[10] Furthermore, an American study on nurses working with patients after a myocardial infarction and national surveys in Ireland and Sweden of cardiac rehabilitation centers and coronary care unit teams produced comparable findings.[11,14,16] We can conclude that the lack of discussion about sexual health and the lack of sexual counseling in different cardiac settings constitute a general problem that relates not only to HF nurses, but also other cardiac healthcare providers. This limited implementation of sexual counseling in practice may rightly be called a concern, because a considerable number of patients with HF experience sexual difficulties that exert a negative effect on their own quality of life and that of their partners.[6,17] Patients worry about resuming sexual activity and are in need of education and counseling on the topic of sexual health.[1,2] Furthermore, previous research indicated that patients also experience barriers to initiating this topic.[7]

Therefore, to improve the treatment of cardiac patients, more attention needs to be paid to sexual counseling in nursing education. However, to educate nurses successfully on this subject, it is important to know which barriers keep nurses from assessing sexual health and providing counseling. We found that the most

frequently reported barrier to addressing sexual concerns was the lack of an organizational policy. This finding is a surprising, because HF guidelines recommend that healthcare providers assess sexual health with both male and female patients and their partners.[8,9] The current class of recommendation assigned to this subject is "I", which indicates that counseling on sexual activity is considered very important. However, the results of our study suggest that HF clinics in The Netherlands do not pursue a policy that ensuring that patients are structurally educated and counseled on this subject. To improve the discussion of sexual health with patients, a first step could involve implementing these guidelines in treatment protocols.

We found subtle differences in barriers perceived by nurses who do and nurses who do not discuss sexual health with their patients. Nurses who do discuss sexual health experience more barriers related to patient factors, such as issues related to culture, religion, language, ethnicity, severity of illness, and the nurses' belief that the patient does not see sexuality as a problem. On the other hand, nurses who do not discuss sexual health experience more barriers related to external factors, such as a lack of training, a lack of general knowledge, a lack of knowledge on how to initiate the topic, and the fact that the patient does not initiate the subject. In addition, nurses who do discuss sexual health with their patients more often reported to going on to higher education regarding sexual counseling. When considering these differences in barriers, to improve treatment, nurses may benefit from specific training courses to help them gain more knowledge about sexual health, acquire communication skills, and to feel more comfortable discussing this topic.

Furthermore, it might help nurses to discuss sexual health at a moment most comfortable for them. According to our findings this moment occurs during a follow-up visit at the HF clinic, or when medication is discussed. This result confirms our finding that nurses working at HF clinics believe they are responsible for assessing sexuality; they do not delegate this task to their colleagues working at the rehabilitation centers. Nurses could use validated questionnaires to initiate the topic of sexual health, or they could try to address the topic while discussing

medications with the patients.[18] The moment when a medication (eg, beta-blockers) is uptitrated provides the perfect opportunity for nurses to enquire after changes in sexual responses or fear of impotence. Nurses may also benefit from a practical workshop where they could practice the approach that would suit them best. Furthermore, such programs would be more helpful if they addressed the roles that different team members play in assessing sexuality and providing sexual counseling to patients. Taking these educational courses can be advantageous, because the improved knowledge and attitudes of nurses will help them feel at ease when discussing sexual health in practice.[19] Steinke et al. suggested a number of strategies that can be used in patient education and management.[20] For example, they suggest to initiate the topic of sexual health after discussing exercise recommendations. To this end, they recommend using a general statement, eg, "Many individuals with HF have questions and concerns about resuming sexual activity. What concerns do you have?" In addition, Mick offered 10 strategies to help nurses who work with oncology patients address and validate patients' sexual experiences and concerns about quality of life.[21] Such strategies could easily be translated to cardiology practice. The strategies by Mick for nurses to understand sexuality include providing information, addressing causes of discomfort, and listening objectively.[21]

A limitation of this study involves the generalizability its results. We are aware of the fact that our study sample may be too homogenous. For instance, we sent 3 copies of the questionnaire to all HF clinics in The Netherlands, but did not direct the questionnaires to the nurses personally. We expected the response to be higher if the questionnaires were addressed anonymously. However, as a consequence of this approach, we only acquired information on the demographics of nurses who did respond, and thus there was a lack of information on nurses who did not respond. Furthermore, we can reasonably expect that, for the most part, nurses who already have an affinity with the subject completed and returned the questionnaire. This could have resulted in an overrepresentation of the percentage of nurses who not only feel responsible for addressing the topic of sexual health, but who also put this responsibility into practice. Furthermore, we imagine that

nurses who do not recognize the importance of the subject, and who therefore do not feel responsible for discussing sexual health with their patients, also did not complete the questionnaire. Our study was also limited because we did not perform psychometric testing on the complete questionnaire; we only tested for face-validity. Although the questionnaires were previously used in a European population, they were not primarily developed for the Dutch population.[8]

We can conclude that although nurses feel they have a responsibility to discuss their patients' sexual health, sexuality is rarely discussed in HF clinics. The preferred moment of initiating this topic occurs during a follow-up visit to the outpatient clinic or when medication is discussed. Barriers experienced by nurses to discussing sexuality are related to personal, patient and organizational factors.

To improve patient care, interventions and training courses should focus on improving both nurses' knowledge about sexual health and their communication skills. Such educational courses should be practical and aimed at making nurses feel at ease discussing matters of sexuality in daily practice. The roles of different team members and the possibilities for referral to other professions also need to be taken into account. Furthermore, HF guidelines should include sexual counseling in the policy of organizations.

Acknowledgements

The authors are grateful to the HF nurses who took the time to participate in this research. We would like to thank the steering committee members for their help: R.Y. Schouten, J.M.A. Visser-Meily, P. Ninaber, J.E. de Groot, C.C. Tuijnman-Raasveld, K. Kanselaar, P. Rabsztyn and W.J. Louridtz.

References

1. Jaarsma T. Sexual problems in heart failure patients. *Eur J Cardiovasc Nurs* 2002;1:61-67.
2. Jaarsma T, Dracup K, Walden J, Stevenson LW. Sexual function in patients with advanced heart failure. *Heart Lung* 1996;**25**:262-270.
3. Mandras SA, Uber PA, Mehra MR. Sexual activity in chronic heart failure. *Mayo Clin Proc* 2007;**82**:1203-1210.
4. Rosen RC, Kostis JB, Jekelis A, Taska LS. Sexual sequelae of antihypertensive drugs: treatment effects on self-report and physiological measures in middle-aged male hypertensives. *Arch Sex Behav* 1994;**23**:135-152.
5. Silvestri A, Galetta P, Cerquetani E, Marazzi G, Patrizi R, Fini M, Rosano GM. Report of erectile dysfunction after therapy with beta-blockers is related to patient knowledge of side effects and is reversed by placebo. *Eur Heart J* 2003;**24**:1928-1932.
6. Westlake C, Dracup K, Walden JA, Fonarow G. Sexuality of patients with advanced heart failure and their spouses or partners. *J Heart Lung Transplant* 1999;**18**:1133-1138.
7. Gott M. Hinchliff S. Barriers to seeking treatment for sexual problems in primary care: a qualitative study with older people. *Fam Pract* 2003;**20**:690-695.
8. Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008. *Eur J Heart Fail* 2008;**10**:933-989.
9. Heart Failure Society Of America. HFSA 2006 Comprehensive Heart Failure Practice Guideline. *J Card Fail* 2006;**12**:10-38.
10. Jaarsma T, Strömberg A, Fridlund B, De Geest S, Mårtensson J, Moons P, et al. Sexual counselling of cardiac patients: nurses' perception of practice, responsibility and confidence. *Eur J Cardiovasc Nurs* 2010;**9**:24-29.

11. Doherty S, Byrne M, Murphy AW, McGee HM. Cardiac rehabilitation staff views about discussing sexual issues with coronary heart disease patients: a national survey in Ireland. *Eur J Cardiovasc Nurs* 2011;**10**:101-107.
12. Jaarsma T, Tan B, Bos RJ, van Veldhuisen DJ. Heart failure clinics in the Netherlands in 2003. *Eur J Cardiovasc Nurs* 2004;**3**:271-274.
13. Jaarsma T, Haaijer-Ruskamp FM, Sturm H, Van Veldhuisen DJ. Management of heart failure in The Netherlands. *Eur J Heart Fail* 2005;**7**:371-375.
14. Steinke EE, Patterson-Midgley P. Sexual counselling of MI patients: nurses' comfort, responsibility, and practice. *Dimens Crit Care Nurs* 1996;**15**:216–223.
15. Waterhouse JK. *Development and testing of a structural equation model of nursing practice related to sexuality*. Doctoral dissertation. University of Delaware, Newark, DE; 1996.
16. Ivarsson B, Fridlund B, Sjöberg T. Information from health care professionals about sexual function and coexistence after myocardial infarction: a national survey. *Heart Lung* 2009;**38**:3350-3355.
17. Hoekstra T, Jaarsma T, Sanderman R, van Veldhuisen DJ, Lesman-Leegte I. Perceived sexual difficulties and associated factors in patients with heart failure. *Am Heart J* 2012;**163**:246-251.
18. Jaarsma T, Steinke EE, Gianotten WL. Sexual problems in cardiac patients: how to assess, when to refer. *J Cardiovasc Nurs* 2010;**25**:159-164.
19. Post MWM, Gianotten WL, Heijnen L, Lambers EJHR, Willems M. Sexological competence of different rehabilitation disciplines and effects of a discipline-specific sexological training. *Sex Disabil* 2008;**26**:3-14.
20. Steinke EE, Mosack V, Wright DW, Chung ML, Moser DK. Risk factors as predictors of sexual activity in heart failure. *Dimens Crit Care Nurs* 2009;**28**:123-129.
21. Mick JM. Sexuality assessment: 10 Strategies for improvement. *Clin J Oncol Nurs* 2007;**11**:671-675.

Chapter 8:
Summary, conclusions, and future perspectives

Summary, conclusions, and future perspectives

The aims of this thesis were twofold: firstly, to gain more insight in the quality of life of patients with heart failure, more specifically those patients with heart failure and a preserved ejection fraction (HF-PEF), and secondly, to learn more about the sexual health of patients with heart failure. In recent years, studies on patient-centred outcomes, such as quality of life, have become of great importance, particularly because life expectancies for patients with heart failure have increased and patients have to adjust to living with a chronic condition.[1,2] Fortunately, due to recent research on this topic, knowledge of quality of life, and more importantly, knowledge of how to improve quality of life of patients with heart failure, is increasing. Nevertheless, there are still some gaps in this research area that need to be addressed. Not only is the knowledge of the quality of life of patients with heart failure and a preserved ejection fraction (HF-PEF) limited, but sexual health is also rarely addressed; even though this is an important component of quality of life of both men and women with cardiovascular disease.[3] This is remarkable, because about 50% of all patients with heart failure have HF-PEF,[4,5] and at least 50% of all patients with heart failure report their sexual activity has decreased or completely ceased as a result of their heart failure.[6-9] The first part of this thesis looked at the prognostic value of quality of life of patients with heart failure, and in particular the quality of life of patients with HF-PEF. The second part of the thesis focused on the sexual health of patients with heart failure and the current practice of discussing sexuality by heart failure nurses.

PART I

To examine the prognostic value of quality of life on long-term survival of patients with heart failure

Main findings

Chapter 2 showed that the quality of life of heart failure patients assessed at discharge from the hospital, is a predictor for 3-year mortality, independent of disease severity, measured by plasma B-type natriuretic peptide (BNP) levels, and a wide range of demographical and clinical variables. General health and physical functioning, assessed with a disease-generic quality of life questionnaire, can provide prognostic information on survival in addition to other prognostic variables. Patients with low scores on these dimensions were more likely to be in New York Heart Association (NYHA) functional class III-IV, were diagnosed with co-morbidities, were suffering from heart failure longer, had lower estimated glomerular filtration rates (eGFR's), and had fewer beta-blocker prescriptions.

To examine the quality of life of patients with heart failure and a preserved left ventricular ejection fraction in more detail

Main findings

Chapters 3 and 4 focused on the quality of life of patients with HF-PEF. Chapter 3 reported that the quality of life of patients with HF-PEF and elevated plasma BNP levels was similarly impaired when compared with age- and gender-matched patients with heart failure and a reduced ejection fraction (HF-REF). In Chapter 4, patients with a preserved ejection fraction and plasma BNP levels >100pg/ml were compared with patients with a preserved ejection fraction and plasma BNP levels <100pg/ml. Patients with a preserved ejection fraction and BNP levels <100pg/ml, did not differ from patients with HF-PEF and BNP levels >100pg/ml on a broad range of characteristics and HF symptoms. The former were, however, more often obese and in NYHA class III-IV. Furthermore, their quality of life was just as impaired as the quality of life of patients with HF-PEF and BNP levels >100pg/ml. Although there is a clinically relevant difference in

the scores indicating worse disease-generic quality of life on the physical functioning, general health and bodily pain dimensions for patients with BNP levels <100pg/ml.

Part I: Conclusion and discussion

The quality of life of patients with HF-PEF, irrespective of their plasma BNP levels, proved to be similar to patients with HF-REF. Quality of life, in particular physical functioning and general health, was related to long-term survival of these patients. Therefore, interventions should focus on improving (physical) quality of life in order to improve both long-term survival and to increase patients' zest for living. These interventions might include offering education to patients on the importance of exercise, referring patients to a rehabilitation centre, and enrolling patients in exercise programmes. Patients can also adopt a more physically active lifestyle by integrating exercise in their daily activities, for instance, by taking a brisk walk, climbing stairs (rather than taking the lift), doing more housework, gardening, and engaging in active recreational pursuits.[10] Several studies have demonstrated that exercise training is safe and can improve the quality of life of patients with heart failure.[11-13] When attending an exercise programme, an individualised approach that includes a clinical evaluation that takes into account behavioural characteristics, personal goals, and preferences is recommended.[14] Individualised training protocols can vary on a number of factors: intensity (aerobic and anaerobic), type (endurance, resistance, and strength), method (continuous and intermittent/interval), application (systematic, regional, and respiratory muscle), control (supervised and non-supervised), and setting (hospital/centre- and home-based).[14,15]

PART II

To assess the prevalence of sexual problems and related factors in patients with heart failure

Main findings

Chapter 5 showed that almost 50% of the patients with heart failure perceived difficulties with sexuality at one month after hospital discharge. Thirty percent recovered from these difficulties during a 17-month follow-up period. However, about the same number of patients developed sexual problems during this period. Experiencing sexual difficulties was independently associated with a lower physical and emotional quality of life. Chapter 6 reported that, compared with healthy community controls, younger patients and patients with a partner experienced more sexual problems. Although male patients more often perceived sexual problems, a large number of women, older patients, and patients without a partner also reported sexual problems. A considerable number of patients with heart failure attributed their sexual problems to symptoms of heart failure, including dyspnoea, fatigue, and exercise intolerance.

To describe the current practice of discussing sexuality by heart failure nurses

Main findings

Chapter 7 observed that the majority of the heart failure nurses felt responsible for discussing sexual health. However, in daily practice sexuality was rarely discussed with patients with heart failure. Nurses who did discuss sexuality with their patients more often reported that they had attended courses on sexual counselling. The most prominent barriers experienced by nurses who did not discuss sexual health were lack of an organisational policy, lack of training, not knowing how to initiate the subject, and the fact that patients do not initiate the topic themselves.

Part II: Conclusion and discussion

Chapters 5 and 6 demonstrated that a large proportion of male and female patients, regardless of age and marital status, reported sexual problems at 1 and 17 months after hospital discharge. Having sexual problems was related to a lower

quality of life, and patients attributed these problems to their disease. This implies that sexual health needs to be discussed during treatment, preferably more than once, with both male and female patients, regardless of whether they have a partner. Although nurses feel they have a responsibility to discuss sexual health with their patients, Chapter 7 noted that in daily practice sexual health was in fact rarely discussed with patients with heart failure. Although these findings are comparable with results of previous studies on the feelings of responsibility of cardiac healthcare providers and the practice of discussing sexual health in cardiac settings, they are nevertheless remarkable.[16 20] Heart failure guidelines explicitly recommend that healthcare providers should assess sexual health with both male and female patients and their partners.[21,22] Recently, a scientific statement on sexual activity and cardiovascular disease has been published.[23] This document stated that approximately 60% to 87% of patients with heart failure report sexual problems.[6-8] However, something can be done about these alarmingly high figures. An optimal treatment of heart failure, for instance, can increase the likelihood of safe and satisfactory sexual activity. Studies on stable patients with heart failure have shown that it is safe for such patients to engage in sexual activity.[24-27] Furthermore, exercise training improves quality of life, and may have a positive impact on the sexual health of patients with heart failure as well.[12,28]

Critical reflection on study population and methodology

In the previous chapters, limitations and methodological considerations specific to this particular study were described. In this section a critical reflection on some methodological issues of this thesis is presented.

Data of patients participating in the COACH study (Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure) were used for the studies described in Chapters 2 to 6.[29,30] The COACH study is one of the largest of its kind to evaluate the role of advice and counselling in patients with heart failure. A total of 1023 patients were randomized and followed for 18 months. The selection criteria for the patient population were broad, and the diagnosis of heart failure

was based on the 2001 guidelines.[31] This resulted in a study sample of elderly patients with several co-morbidities, as well as patients with HF-REF and HF-PEF, with both high and low plasma BNP levels. The heart failure study population is representative of the heart failure population seen in clinical practice and outpatient clinics. Therefore, results can be generalised to the clinical heart failure population. However, to minimize the at times severe impact of a recent hospitalization on quality of life and sexual health, data on these variables were used at 1 and 18 months after discharge in the studies described in Chapters 3, 4, 5, and 6.

The studies included in this thesis that use data of the patients participating in the COACH study (Chapters 2 to 6) were secondary group analyses. The COACH study was not primarily designed to investigate the prognostic value of quality of life on survival, the quality of life in patient with HF-PEF and HF-REF, and sexual problems in patients with heart failure.

Implications for health care

Improving physical functioning

The findings of this thesis show that quality of life is low in patients with heart failure. Additionally, physical functioning is independently associated with mortality (Chapter 2) and related to sexual problems (Chapter 5). Therefore, to increase the quality of life and survival of these patients, improving physical function should form an important component of the treatment programmes for these patients, along with offering education on how to live with a chronic disease like heart failure, and helping patients set realistic goals to improve their quality of life in other domains than physical functioning.

Studies have shown that exercise training improves physical functioning and quality of life, and reduces mortality in patients with heart failure, including patients with HF-PEF.[20,32,33] In addition, the heart failure guidelines recommend regular physical activity and structured exercise training for these patients.[20] Unfortunately, according to a European survey, less than 20% of the patients with

heart failure are currently participating in a cardiac rehabilitation programme.[34] In The Netherlands only 3.7% of the patients with heart failure is referred to a rehabilitation centre.[35] Therefore, it is important to develop strategies that improve referral to cardiac rehabilitation centres. Possible strategies could include increasing the awareness of healthcare providers working with patients with heart failure about the possibility to refer patients to cardiac rehabilitation centres, the benefits of exercise training, and the recommendations of the guidelines. Furthermore, cardiac rehabilitation centres might want to inform nearby heart failure clinics about the exercise programmes they offer.

Improving physical functioning: implications for healthcare providers

Considering the importance of improving physical functioning, it is vital that healthcare providers working at heart failure clinics recognise which patients could benefit from exercise training. The guidelines recommend exercise training for stable patients with heart failure, who are in NYHA functional class I-III.[20] However, patients with advanced or acute heart failure may also benefit from exercise training after hospital admission. It might prevent them from further disability, and lay the foundations for the formal exercise training plan.[14] This means that a broad range of patients could benefit from an exercise training programme, particularly patients with low physical functioning. In order to single out patients with low physical functioning, healthcare providers could ask patients to complete a questionnaire on physical functioning, for example, the particular subscale of the RAND36 questionnaire, prior to their first visit to the heart failure clinic. The healthcare provider should educate all patients about the importance of regular exercise, and when the current level of physical functioning is low, refer them to a cardiac rehabilitation centre where they can obtain a suitable exercise programme.

Healthcare providers should, however, keep in mind that patients who have depressive symptoms do not benefit from interventions.[36] Therefore, it is important to assess depressive symptoms in addition to physical functioning, for example, with an interview or the CES-D questionnaire. Unfortunately, an overlap

exists between depressive symptoms and heart failure symptoms. To reveal the underlying cause, healthcare providers therefore need to discuss the results of the questionnaire with their patients. When the symptoms appear to be depression-related, and not heart failure-related, in addition to improving their physical functioning, patents should also be referred to a psychologist.

Discussing sexual health

Prior studies have shown that compliance with the heart failure regimen is related to the knowledge patients have of heart failure and the prescribed regimen.[37] Improving knowledge by means of education and counselling remains an important issue in heart failure disease management programs, and a comprehensive nursing assessment is essential in this respect.[20] This assessment should focus on education about the consequences of heart failure, heart failure symptoms, and the regimen, which includes the effect of heart failure and heart failure medication on sexuality. Although heart failure nurses feel responsible for discussing sexuality with their patients, the majority of the nurses do not assess sexual health in practice (Chapter 7). This limited counselling on sexuality may rightfully be called a concern, because a considerable number of patients with heart failure experience difficulties with sexuality, which in turn have a negative influence on their quality of life (Chapter 5). This thesis has shown that the most prominent barrier that keeps nurses from sexual counselling is the lack of organisational policy, which means that a discussion of sexual health is not included in the treatment protocols of heart failure clinics. This is surprising, because the heart failure guidelines recommend discussing sexual health with all male and female patients and their partners.[20] Therefore, the first step towards improving counselling on sexual problems should include encouraging the management team of heart failure clinics to integrate a discussion of sexual health in their treatment protocol.

Discussing sexual health: implications for healthcare providers

The second barrier mentioned by nurses with respect to discussing sexual health relates to the lack of training they experience (Chapter 7). Due to economising on hospital resources, nurses often suffer from cutbacks on education. However, nurses might benefit from an interactive course which not only focuses on increasing knowledge on how heart failure and medication affect sexuality, but also helps nurses with practical exercises on how to initiate the subject. Such a course enables nurses to gain knowledge, but also helps them acquire the kind of communication skills that will make them feel more comfortable discussing a sensitive subject such as sexual health. Training on how to approach a subject like sexual health can definitely be an incentive to nurses to start discussing sexual health with their patients.

An easy way to broach the subject is by informing patients that the symptoms of heart failure and the medication regimen will affect many aspects of their lives, including sexual functioning. This creates an environment where patients feel more comfortable to talk about their concerns. Furthermore, the healthcare provider should keep in mind that a number of patients experiencing sexual difficulties 1 month after discharge, recovers from these difficulties during a 17-months follow-up period. However, around the same number of patients who did not experience difficulties at 1 month after discharge, develop these during the follow-up period (Chapter 5). Therefore, healthcare providers should inform patients about the possibility to discuss sexual health more than once during the treatment period.

If the treatment of the specific sexual problem lies beyond the scope of the healthcare provider working at the heart failure clinic, he or she should be aware of the possibility to refer the patient to a psychologist, sexologist, or urologist. Heart failure clinics could benefit from an organisation chart in which the patient with heart failure has a central role. By adding all healthcare providers and their specific expertise related to sexual problems to this chart, referral will become easier and less time-consuming for both the healthcare provider and the patients.

Implications for further research

Patients with heart failure with preserved ejection fraction

Pharmacological and non-pharmacological management interventions have proven to be successful in patients with HF-REF. They increase survival rates, decrease morbidity rates, and improve quality of life. Unfortunately, there are no treatment options for patients with HF-PEF that have proven to be effective over a longer period of time. Pharmacological interventions that are successful in patients with HF-REF, for instance, have shown to be ineffective in patients with HF-PEF.[38-41] This suggests that HF-PEF differs in pathology from HF-REF. In order to find a suitable medical treatment for patients with HF-PEF, it is important to gain insight in the definition and diagnosis of this disease. Therefore, future research should not only focus on successful (pharmacological and non-pharmacological) interventions to improve survival and quality of life of patients with HF-PEF, but also look at the cause and development of HF-PEF and the interaction with high age and co-morbidities of the patients.

Improving sexual health

This thesis has observed that many patients with heart failure experience sexual problems. Future research could focus on how to improve the sexual health of these patients. A variety of studies have been conducted on how to treat erectile dysfunction in male patients with heart failure, and on the effect of phosphodiesterase type 5 inhibitors in these patients.[42] However, there are no studies to date that address sexual problems in female heart failure patients, or that focus on other sexual problems than erectile dysfunction in patients with heart failure. Therefore, future research on improving sexual health in patients with heart failure should focus on these aspects as well. Possible research interventions for improving sexuality could include sexual counselling by using the PLISSIT (permission, limited information, specific suggestion, and intensive therapy) model. This model is a practical and useful tool that helps healthcare providers in their discussion of sexual health with their patients.[43-45]

References

1. Murdoch DR, Love MP, Robb SD, et al. Importance of heart failure as a cause of death. Changing contribution to overall mortality and coronary heart disease mortality in Scotland 1979-1992. *Eur Heart J* 1998;**19**:1829-1835.
2. Najafi F, Dobson AJ, Jamrozik K. Is mortality from heart failure increasing in Australia? An analysis of official data on mortality for 1997-2003. *Bull World Health Organ* 2006;**84**:722-728.
3. Lindau ST, Schumm LP, Laumann EO, Levinson W, O'Muircheartaigh CA, Waite LJ. A study of sexuality and health among older adults in the United States. *N Engl J Med* 2007;**357**:762-774.
4. Kindermann M, Reil JC, Pieske B, et al. Heart failure with normal left ventricular ejection fraction: what is the evidence? *Trends Cardiovasc Med* 2008; **18**:280-292.
5. Paulus WJ, van Ballegoij JJ. Treatment of heart failure with normal ejection fraction: an inconvenient truth! *J Am Coll Cardiol* 2010; **55**:526-537.
6. Jaarsma T, Dracup K, Walden J, et al. Sexual function in patients with advanced heart failure. *Heart Lung* 1996;**25**:262-270.
7. Schwarz ER, Kapur V, Bionat S, et al. The prevalence and clinical relevance of sexual dysfunctioning in women and men with chronic heart failure. *Int J Impot Res* 2008;**20**:85-91.
8. Jaarsma T. Sexual problems in heart failure patients. *Eur J Cardiovasc Nurs* 2002;**1**:61-67.
9. Westlake C, Dracup K, Walden JA, et al. Sexuality op patients with advanced heart failure and their spouses or partners. *J Heart Lung Transplant* 1999;**18**:1133-1138.
10. Piepoli MC, Corrà U, Benzer W, et al. Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2010;**17**:1-17.

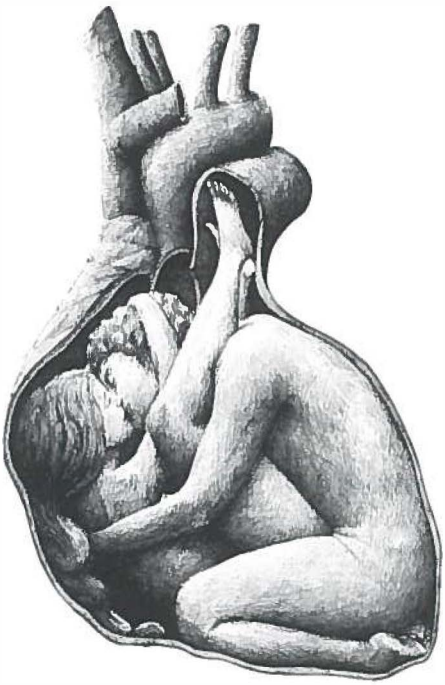
11. Davis EJ, Moxham T, Rees K, et al. Exercise training for systolic heart failure: Cochrane systematic review and meta-analysis. *Eur J Heart Fail* 2010;**12**:706-715.
12. Flynn KE, Pina IL, Whellan DJ, et al. Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009;**301**:1451-1459.
13. O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients iwht chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009;**301**:1439-1450.
14. Piepoli MF, Conraads V, Corrà U, et al. Exercise training in heart failure: from theory to practice. A consensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation. *Eur J Heart Fail* 2011;**13**:347-357.
15. Gielen S, Niebauer J, Hambrecht R. *Exercise training in heart failure.* In: Perk J, Mathes P, Gohlke H, et al. Cardiovascular Prevention and Rehabilitation. London: Springer; 2007.
16. Jaarsma T, Strömberg A, Fridlund B, et al. Sexual counselling of cardiac patients: nurses' perception of practice, responsibility and confidence. *Eur J Cardiovasc Nurs* 2010;**9**:24-29.
17. Doherty S, Byrne M, Murphy AW, McGee HM. Cardiac rehabilitation staff views about discussing sexual issues with coronary heart disease patients: a national survey in Ireland. *Eur J Cardiovasc Nurs* 2011;**10**:101-107.
18. Steinke EE, Patterson-Midgley P. Sexual counselling of MI patients: nurses' comfort, responsibility, and practice. *Dimens Crit Care Nurs.* 1996;**15**:216-223.
19. Ivarsson B, Fridlund B, Sjöberg T. Information from health care professionals about sexual function and coexistence after myocardial infarction: a national survey. *Heart Lung* 2009;**38**:3350-3355.
20. Goossens E, Norekvål TM, Faerch J, et al. Sexual counselling of cardiac patients in Europe: culture matters. *Int J Clin Pract* 2011;**65**:1092-1099.

21. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. *Eur J Heart Fail* 2008;**10**:933-989.
22. Heart Failure Society of America. HFSA 2006 Comprehensive Heart Failure Practice Guideline. *J Card Fail* 2006;**12**:10-38.
23. Levine GN, Steinke EE, Bakaeen FG, et al. Sexual activity and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation* 2012;**125**:1058-1072.
24. Bocchi EA, Guimarães G, Mocelin A, Bascal F, Belotti G, Ramires JF. Sildenafil effects on exercise, neurohormonal activation, and erectile dysfunction in congestive heart failure: a double-blind, placebo-controlled, randomized study followed by a prospective treatment for erectile dysfunction. *Circulation* 2002;**106**:1097-1103.
25. Freitas D, Athanazio R, Almeida D, Dantas N, Reis F. Sildenafil improves quality of life in men with heart failure and erectile dysfunction. *Int J Impot Res* 2006;**18**:210-212.
26. Katz SD, Parker JD, Glasser DB, et al. Efficacy and safety of sildenafil citrate in men with erectile dysfunction and chronic heart failure. *Am J Cardiol* 2005;**95**:36-42.
27. Webster LJ, Michelakis ED, Davis T, Archer SL. Use of sildenafil for safe improvement of erectile function and quality of life in men with New York Heart Association classes II and III congestive heart failure: a prospective, placebo-controlled, double-blind crossover trial. *Arch Intern Med* 2004;**164**:514-520.
28. Belardinelli R, Lacalaprice F, Faccenda E, Purcaro A, Perna G. Effects of short-term moderate exercise training on sexual function in male patients with chronic stable heart failure. *Int J Cardiol* 2005;**101**:83-90.

29. Jaarsma T, Van Der Wal MH, Hogenhuis J, et al. Design and methodology of the COACH study: a multicenter randomised Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure. *Eur J Heart Fail* 2004;**6**:227-233.
30. Jaarsma T, van der Wal MH, Lesman-Leegte I, et al. Effect of moderate or intensive disease management program on outcome in patients with heart failure: Coordinating Study Evaluating Outcomes of Advising and Counselling in Heart Failure (COACH). *Arch Intern Med* 2008;**168**:316-324.
31. Remme WJ, Swedberg K. Guidelines for the diagnosis and treatment of chronic heart failure. *Eur Heart J* 2001;**22**:1527-1560.
32. Edelmann F, Gelbrich G, Düngen HD, et al. Exercise training improves exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction: results of the Ex-DHF (Exercise training in Diastolic Heart Failure) pilot study. *J Am Coll Cardiol* 2011;**58**:1780-1791.
33. Kitzman DW, Brubaker PH, Morgan TM, et al. Exercise training in older patients with heart failure and preserved ejection fraction: a randomized controlled, single-blind trial. *Circ Heart Fail* 2010;**3**:659-667.
34. Bjarnason-Wehrens B, McGee H, Zwisler AD, et al. Cardiac rehabilitation in Europe: results from the European Cardiac Rehabilitation Inventory Survey. *Eur J Cardiovasc Prev Rehabil* 2010;17:410-418.
35. van Engen-Verheul M, de Vries H, Kemps H, et al. Cardiac rehabilitation uptake and its determinants in the Netherlands. *Eur J Prev Cardiol* 2012 [Epub ahead of print].
36. Jaarsma T, Lesman-Leegte I, Hillege HL, et al. Depression and the usefulness of a disease management program in heart failure: insights from the COACH (Coordinating study evaluating Outcomes of Advising and Counseling in Heart failure) study. *J Am Coll Cardiol* 2010;**55**:1837-1843.
37. van der Wal MH, Jaarsma T, Moser DK, et al. Compliance in heart failure patients: the importance of knowledge and beliefs. *Eur Heart J* 2006;**27**:434-440.

38. Yusuf S, Pfeffer MA, Swedberg K, et al. Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: The CHARM-Preserved Trial. *Lancet* 2003;**362**:777-781.
39. Massie BM, Carson PE, McMurray JJ, et al. Irbesartan in patients with heart failure and preserved ejection fraction. *N Engl J Med* 2008;**359**:2456-2467.
40. Cleland JGF, Tendera M, Adamus J, Freemantle N, Polonski L, Taylor J. The perindopril in elderly people with chronic heart failure (PEP-CHF) study. *Eur Heart J* 2006;**27**:2338-2345.
41. Yamamoto K, Sakata Y, Ohtani T, Takeda Y, Mano T. Heart failure with preserved ejection fraction. *Circ J* 2009;**73**:404-410.
42. Al-Ameri H, Kloner RA. Erectile dysfunction and heart failure: the role of phosphodiesterase type 5 inhibitors. *Int J Impot Res* 2009;**21**:149-157.
43. Jaarsma T, Steinke EE, Gianotten WL. Sexual problems in cardiac patients: how to assess, when to refer. *J Cardiovasc Nurs* 2010;**25**:159-164.
44. Annon J. The PLISSIT model: a proposed conceptual scheme for the behavioural treatment of sexual problems. *J Sex Educ Ther* 1976;**2**:1-15.
45. Taylor B, Davis S. Using the extended PLISSIT model to address sexual healthcare needs. *Nurs Stand* 2006;**21**:35-40.

Samenvatting en conclusies



Samenvatting en conclusies

Het doel van dit proefschrift was om meer inzicht in de kwaliteit van leven van patiënten met hartfalen te verkrijgen, in het bijzonder in de kwaliteit van leven van patiënten met hartfalen en een behouden linker ventrikel ejectie fractie (heart failure with a preserved ejection fraction, HF-PEF). Daarnaast is er uitgebreid aandacht besteed aan de seksuele problemen van patiënten in relatie tot hun hartfalen. Omdat de levensverwachting van patiënten met hartfalen is toegenomen, en patiënten moeten leren leven met een chronische aandoening, wordt er steeds meer belang gehecht aan studies naar patiënt gerelateerde uitkomsten.[1,2] Door onderzoek naar dit onderwerp te verrichten is niet alleen de kennis over de kwaliteit van leven toegenomen, maar ook de kennis over hoe deze kwaliteit verbeterd kan worden bij patiënten met hartfalen. Helaas is er ook nog veel niet bekend op dit gebied: niet alleen is de kennis over de kwaliteit van leven van patiënten met hartfalen en een behouden ejectie fractie minimaal, maar ook seksuele gezondheid, toch een belangrijk onderdeel van de kwaliteit van leven van mannen en vrouwen met een cardiovasculaire aandoening, krijgt maar weinig aandacht.[3] Dit mag met recht opvallend genoemd worden, omdat ongeveer 50% van alle patiënten met hartfalen een behouden ejectie fractie heeft,[4,5] en minstens 50% van alle patiënten met hartfalen rapporteert dat hun seksuele activiteiten zijn afgenomen of zelfs geheel gestopt zijn vanwege hun hartfalen.[6-9] Het eerste deel van het proefschrift onderzocht de voorspellende waarde van kwaliteit van leven op de kans van overlijden van patiënten met hartfalen, en beoogde daarnaast meer inzicht te krijgen in de kwaliteit van leven van patiënten met een behouden ejectie fractie. Het tweede deel van het proefschrift richtte zich op de seksuele gezondheid van patiënten met hartfalen en de huidige praktijk in hartfalen poliklinieken met betrekking tot het bespreken van seksualiteit.

DEEL I

Inzicht krijgen in de voorspellende waarde van kwaliteit van leven op de kans van overlijden op de lange termijn bij patiënten met hartfalen

Belangrijkste resultaten

In hoofdstuk 2 werd aangetoond dat kwaliteit van leven, gemeten bij ontslag na een ziekenhuisopname voor hartfalen, een voorspellende waarde heeft in relatie tot de kans op overlijden binnen 3 jaar na ontslag, onafhankelijk van de ziekte-ernst, gemeten met bloedwaarden van B-type natriuretic peptide (BNP), en een groot aantal demografische en klinische variabelen. Vooral de algemene gezondheid en het fysieke functioneren, gemeten met een ziektegenerieke kwaliteit van leven vragenlijst, bleken een voorspellende waarde te hebben ten aanzien van overlijden, aanvullend op andere voorspellende factoren. Patiënten met een lage score op deze subschalen waren vaker ingedeeld in New York Heart Association (NYHA) klasse III-IV, waren vaker gediagnosticeerd met comorbiditeiten, waren sinds langere tijd bekend met de diagnose hartfalen, hadden lagere estimated glomerular filtration rates (eGFR's), en kregen minder vaak bètablokkers voorgeschreven.

Inzicht krijgen in de kwaliteit van leven van patiënten met hartfalen en een behouden ejectie fractie

Belangrijkste resultaten

In hoofdstuk 3 en hoofdstuk 4 werd gekeken naar de kwaliteit van leven van patiënten met hartfalen en een behouden ejectie fractie. Hoofdstuk 3 maakte duidelijk dat de kwaliteit van leven van patiënten met een behouden ejectie fractie (heart failure with a preserved ejection fraction, HF-PEF) en verhoogde BNP-waarden, even slecht is als de kwaliteit van leven van patiënten met een verlaagde ejectie fractie (heart failure with a reduced ejection fraction, HF-REF), waarbij beide groepen gematched zijn op leeftijd en geslacht. In hoofdstuk 4 werd een groot aantal demografische kenmerken, klinische kenmerken, en indicatoren van kwaliteit van leven van patiënten met HF-PEF en BNP-waarden hoger dan

100pg/ml vergeleken met patiënten met HF-PEF en BNP-waarden lager dan 100pg/ml. Patiënten met HF-PEF en BNP-waarden lager dan 100pg/ml bleken niet te verschillen van patiënten met HF-PEF en BNP-waarden hoger dan 100pg/ml, behalve dan dat de patiënten met BNP-waarden lager dan 100pg/ml vaker obees waren, en vaker waren ingedeeld in NYHA klasse III-IV. Daarnaast ervoeren beide groepen hun kwaliteit van leven als even slecht, hoewel er wel een klinisch relevant verschil in de scores viel uit te maken, wat duidde op een slechtere kwaliteit van leven van patiënten met lagere BNP-waarden ten aanzien van de dimensies van fysiek functioneren, algemene gezondheid, en pijn.

Deel I: Conclusie en discussie

De kwaliteit van leven van patiënten met hartfalen en een behouden ejectie fractie, ongeacht de hoogte van hun BNP-waarden, bleek even slecht te zijn als de kwaliteit van leven van patiënten met hartfalen en een verlaagde ejectie fractie. Kwaliteit van leven, in het bijzonder de dimensies fysiek functioneren en algemene gezondheid, is gerelateerd aan een grotere kans op overlijden op de lange termijn bij deze patiënten. Om deze reden is het belangrijk dat interventies bij deze patiënten zich richten op het verbeteren van de (fysieke) kwaliteit van leven. Hiermee wordt niet alleen de kans op overlijden verlaagd, maar krijgen patiënten ook meer plezier in het leven. Voorbeelden van interventies op dit gebied zijn het geven van voorlichting over het belang van bewegen, het tijdig doorverwijzen naar een revalidatiecentrum, en het aanbieden van een op maat gesneden bewegingsprogramma. Patiënten kunnen zichzelf ook een fysiek actievere levensstijl aanleren door bewegen te integreren in hun dagelijkse bezigheden, zoals stevige wandelingen maken, zoveel mogelijk de trap nemen (in plaats van de lift), meer huishoudelijke taken verrichten, tuinieren, en deelnemen aan recreatieve activiteiten die een flinke fysieke inspanning verlangen.[10] Onderzoek heeft aangetoond dat fysieke training veilig is en de kwaliteit van leven van patiënten met hartfalen kan verbeteren.[11-13] Bij deelname aan een bewegingsprogramma is het sterk aan te raden om te kiezen voor een individuele benadering waarbij een klinische evaluatie is inbegrepen, welke onder andere gericht is op

gedragskenmerken, persoonlijke doelen en voorkeuren.[14] Individuele trainingsprogramma's kunnen verschillen ten aanzien van diverse factoren: intensiteit (aerobisch en anaerobisch), soort (uithoudingsvermogen, weerstandsvermogen, en kracht), methode (continu en met tussenpozen/interval), doel (systematisch, regionaal, en gericht op de ademhalingsspieren), controle (met en zonder supervisie), en setting (ziekenhuis, bij een instelling en thuis).[14,15]

DEEL II

Inzicht krijgen in de prevalentie van seksuele problemen en de daarmee gerelateerde factoren bij patiënten met hartfalen

Belangrijkste resultaten

In hoofdstuk 5 werd aangetoond dat bijna 50% van de patiënten met hartfalen een maand na ontslag uit het ziekenhuis problemen met seksualiteit ervoer. Dertig procent herstelde van deze problemen gedurende een follow-up periode van 17 maanden. Echter, tijdens deze periode ontstonden bij ongeveer hetzelfde aantal patiënten seksuele problemen. Het ervaren van seksuele problemen was onafhankelijk gerelateerd aan een lagere fysieke en emotionele kwaliteit van leven. Hoofdstuk 6 liet zien dat, vergeleken met een groep gezonde personen, jongere patiënten en patiënten met een partner vaker problemen met seksualiteit ervoeren. Hoewel mannelijke patiënten vaker seksuele problemen ondervonden, rapporteerden ook een groot aantal vrouwen, oudere patiënten, en patiënten zonder partner seksuele problemen. Een groot aantal patiënten met hartfalen schreef hun problemen toe aan de symptomen van hartfalen, zoals kortademigheid, vermoeidheid, en een verminderd uithoudingsvermogen.

Het beschrijven van de huidige praktijk rondom het bespreken van seksualiteit door hartfalen verpleegkundigen

Belangrijkste resultaten

In hoofdstuk 7 kwam naar voren dat een meerderheid van de hartfalen verpleegkundigen zich verantwoordelijk voelt voor het bespreken van de seksuele gezondheid van hun patiënten. Desondanks werd seksualiteit in de dagelijkse praktijk zelden besproken met patiënten met hartfalen. Verpleegkundigen die het onderwerp seksualiteit wel bespraken met hun patiënten, rapporteerden vaker dat ze een aanvullende opleiding hebben gevolgd specifiek gericht op seksuele counseling. Verpleegkundigen die seksualiteit niet bespraken noemden een aantal barrières waar ze tegenaan liepen; deze varieerden van organisatorische factoren (het beleid van de instelling is niet gericht op het bespreken van seksualiteit en er is een gebrek aan trainingen op dit gebied), tot communicatiegerichte factoren (onzekerheid over hoe het onderwerp aan te snijden en dat patiënten zelf niet over het onderwerp beginnen).

Deel II: Conclusies en discussie

De resultaten van hoofdstuk 5 en hoofdstuk 6 toonden aan dat een groot deel van de mannelijke en vrouwelijke patiënten, oudere en jongere patiënten, en patiënten met en zonder partner na 1 en na 17 maanden na ontslag uit het ziekenhuis problemen met hun seksualiteit ondervonden. Het ervaren van seksuele problemen is gerelateerd aan een lagere kwaliteit van leven, en patiënten schrijven hun problemen toe aan hun ziekte. Daarom is het van groot belang dat de seksuele gezondheid van patiënten met hartfalen besproken wordt gedurende de behandeling, bij voorkeur meerdere malen, met zowel mannelijke en vrouwelijke patiënten, ongeacht hun relatiestatus (wel of geen partner). Hoewel verpleegkundigen zich wel verantwoordelijk voelen voor het bespreken van seksualiteit met hun patiënten, liet hoofdstuk 7 zien dat in de dagelijkse praktijk seksualiteit zelden besproken wordt met patiënten met hartfalen. Ondanks het feit dat deze resultaten vergelijkbaar zijn met de resultaten van eerdere studies naar de verantwoordelijkheid die hulpverleners ervaren, en de praktijk met betrekking tot

het bespreken van seksualiteit op cardiologische afdelingen, zijn ze toch opvallend te noemen.[16-20] Richtlijnen voor de behandeling van hartfalen raden hulpverleners namelijk aan om seksualiteit met zowel mannelijke als vrouwelijke patiënten en hun partners te bespreken.[21,22] Onlangs is er een wetenschappelijke verklaring gepubliceerd over seksualiteit en cardiovasculaire aandoeningen.[23] Uit deze verklaring blijkt dat maar liefst 60% tot 87% van de patiënten met hartfalen seksuele problemen rapporteren.[6-8] Gelukkig kan hier iets aan gedaan worden. Een optimale behandeling van hartfalen vergroot namelijk de kans op veilige en bevredigende seksuele activiteiten. Onderzoek bij stabiele patiënten met hartfalen toont aan dat het voor deze patiënten veilig is om seksueel actief te zijn.[24-27] Daarnaast vergroot fysieke training de kwaliteit van leven, en heeft het mogelijk ook een positief effect op de seksuele gezondheid van patiënten met hartfalen.[12,28]

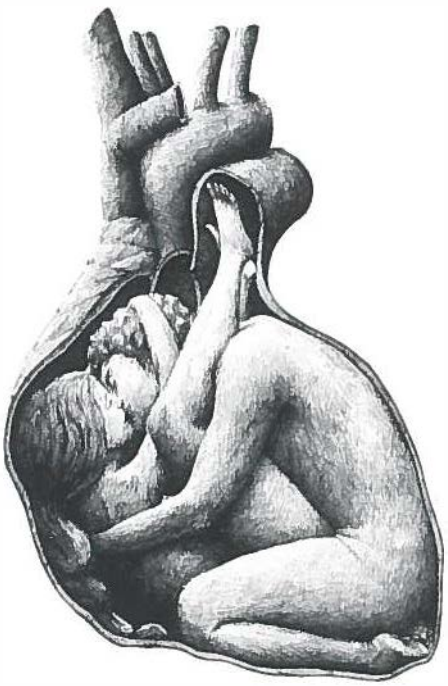
Referenties

1. Murdoch DR, Love MP, Robb SD, et al. Importance of heart failure as a cause of death. Changing contribution to overall mortality and coronary heart disease mortality in Scotland 1979-1992. *Eur Heart J* 1998;**19**:1829-1835.
2. Najafi F, Dobson AJ, Jamrozik K. Is mortality from heart failure increasing in Australia? An analysis of official data on mortality for 1997-2003. *Bull World Health Organ* 2006;**84**:722-728.
3. Lindau ST, Schumm LP, Laumann EO, Levinson W, O'Muircheartaigh CA, Waite LJ. A study of sexuality and health among older adults in the United States. *N Engl J Med* 2007;**357**:762-774.
4. Kindermann M, Reil JC, Pieske B, et al. Heart failure with normal left ventricular ejection fraction: what is the evidence? *Trends Cardiovasc Med* 2008; **18**:280-292.
5. Paulus WJ, van Ballegoij JJ. Treatment of heart failure with normal ejection fraction: an inconvenient truth! *J Am Coll Cardiol* 2010; **55**:526-537.
6. Jaarsma T, Dracup K, Walden J, et al. Sexual function in patients with advanced heart failure. *Heart Lung* 1996;**25**:262-270.
7. Schwarz ER, Kapur V, Bionat S, et al. The prevalence and clinical relevance of sexual dysfunctioning in women and men with chronic heart failure. *Int J Impot Res* 2008;**20**:85-91.
8. Jaarsma T. Sexual problems in heart failure patients. *Eur J Cardiovasc Nurs* 2002;**1**:61-67.
9. Westlake C, Dracup K, Walden JA, et al. Sexuality op patients with advanced heart failure and their spouses or partners. *J Heart Lung Transplant* 1999;**18**:1133-1138.
10. Piepoli MC, Corrà U, Benzer W, et al. Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2010;**17**:1-17.

11. Davis EJ, Moxham T, Rees K, et al. Exercise training for systolic heart failure: Cochrane systematic review and meta-analysis. *Eur J Heart Fail* 2010;**12**:706-715.
12. Flynn KE, Pina IL, Whellan DJ, et al. Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009;**301**:1451-1459.
13. O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients iwht chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009;**301**:1439-1450.
14. Piepoli MF, Conraads V, Corrà U, et al. Exercise training in heart failure: from theory to practice. A consensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation. *Eur J Heart Fail* 2011;**13**:347-357.
15. Gielen S, Niebauer J, Hambrecht R. *Exercise training in heart failure.* In: Perk J, Mathes P, Gohlke H, et al. Cardiovascular Prevention and Rehabilitation. London: Springer; 2007.
16. Jaarsma T, Strömberg A, Fridlund B, et al. Sexual counselling of cardiac patients: nurses' perception of practice, responsibility and confidence. *Eur J Cardiovasc Nurs* 2010;**9**:24-29.
17. Doherty S, Byrne M, Murphy AW, McGee HM. Cardiac rehabilitation staff views about discussing sexual issues with coronary heart disease patients: a national survey in Ireland. *Eur J Cardiovasc Nurs* 2011;**10**:101-107.
18. Steinke EE, Patterson-Midgley P. Sexual counselling of MI patients: nurses' comfort, responsibility, and practice. *Dimens Crit Care Nurs.* 1996;**15**:216-223.
19. Ivarsson B, Fridlund B, Sjöberg T. Information from health care professionals about sexual function and coexistence after myocardial infarction: a national survey. *Heart Lung* 2009;**38**:3350-3355.
20. Goossens E, Norekvål TM, Faerch J, et al. Sexual counselling of cardiac patients in Europe: culture matters. *Int J Clin Pract* 2011;**65**:1092-1099.

21. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. *Eur J Heart Fail* 2008;**10**:933-989.
22. Heart Failure Society of America. HFSA 2006 Comprehensive Heart Failure Practice Guideline. *J Card Fail* 2006;**12**:10-38.
23. Levine GN, Steinke EE, Bakaeen FG, et al. Sexual activity and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation* 2012;**125**:1058-1072.
24. Bocchi EA, Guimarães G, Mocelin A, Bascal F, Belotti G, Ramires JF. Sildenafil effects on exercise, neurohormonal activation, and erectile dysfunction in congestive heart failure: a double-blind, placebo-controlled, randomized study followed by a prospective treatment for erectile dysfunction. *Circulation* 2002;**106**:1097-1103.
25. Freitas D, Athanazio R, Almeida D, Dantas N, Reis F. Sildenafil improves quality of life in men with heart failure and erectile dysfunction. *Int J Impot Res* 2006;**18**:210-212.
26. Katz SD, Parker JD, Glasser DB, et al. Efficacy and safety of sildenafil citrate in men with erectile dysfunction and chronic heart failure. *Am J Cardiol* 2005;**95**:36-42.
27. Webster LJ, Michelakis ED, Davis T, Archer SL. Use of sildenafil for safe improvement of erectile function and quality of life in men with New York Heart Association classes II and III congestive heart failure: a prospective, placebo-controlled, double-blind crossover trial. *Arch Intern Med* 2004;**164**:514-520.
28. Belardinelli R, Lacalaprice F, Faccenda E, Purcaro A, Perna G. Effects of short-term moderate exercise training on sexual function in male patients with chronic stable heart failure. *Int J Cardiol* 2005;**101**:83-90.

Dankwoord



Dankwoord

In februari 2009 ben ik begonnen met mijn promotieonderzoek bij de 'COACH-groep' op de afdeling Cardiologie van het Universitair Medisch Centrum Groningen. Nu, bijna 4 jaar later, is het proefschrift dan ook daadwerkelijk afgerond. Ik kijk met veel plezier terug op een zeer leerzame periode, en ben ik erg dankbaar voor de kans die ik heb gekregen om mijn promotieonderzoek uit te kunnen voeren bij de afdeling Cardiologie van het UMCG.
Ik ben zeer tevreden met het eindresultaat, en had dit niet voor elkaar kunnen krijgen zonder de bijdrage van een groot aantal mensen in mijn omgeving, want promoveren doe je niet alleen. Daarom wil ik hen hierbij bedanken.

Als eerste mijn copromotor dr. I. Lesman-Leegte. Beste Ivonne, jij hebt mij van het begin tot het einde van het promotietraject begeleid. Ik kon altijd op je rekenen als ik er niet uit kwam met de discussie van een artikel, als ik moedeloos werd van de zoveelste versie van een manuscript, en toen ik voor het eerst in het buitenland een presentatie moest geven. Jouw nuchtere kijk op de zaken, je gestructureerde aanpak en je beargumenteerde commentaar hebben mij er de afgelopen jaren door heen geholpen. Ik was jouw eerste promovendus, maar ik had me geen betere copromotor kunnen voorstellen! Heel erg bedankt voor je betrokkenheid, je betrouwbaarheid en je begeleiding.

Mijn promotor prof. dr. D.J. van Veldhuisen. Beste Dirk Jan, ik ben je zeer dankbaar voor de mogelijkheid dat ik, als psycholoog, onderzoek naar de kwaliteit van leven en seksuele problemen bij patiënten met hartfalen op jouw afdeling mocht uitvoeren. Ik heb heel veel van je geleerd, van je grote wetenschappelijk inzicht, je resultaat gerichtheid, en van het denken en schrijven vanuit de 'take-home-message'. Ik wil je bedanken voor je altijd snelle reacties op mijn artikelen, en je concrete commentaar.

Mijn promotor prof. dr. T. Jaarsma. Beste Tiny, ik weet nog heel goed dat ik na mijn eerste sollicitatiegesprek met jou enthousiast over de functie, over het

onderzoek en over de mogelijkheden de kamer uit liep. Alle gesprekken die daar in de afgelopen jaren op volgden, hadden precies hetzelfde effect op mij. Ik bewonder je enthousiasme en je positieve kijk op de zaken, dit werkt zeer aanstekelijk waardoor elke dip na een gesprek met jou volledig was verdwenen en omgebogen naar nieuwe kansen en wegen. Ik heb veel van je geleerd, van je doorzettingsvermogen, van je inzichten, van je kritische (maar nooit negatieve) feedback, je stimulerende houding. Ik ben je heel dankbaar dat je mijn promotor wilde blijven, ook nadat je het UMCG verlaten had voor de functie van professor bij Linköppings Universitet. En ik dank je in het bijzonder dat je mij de kans hebt gegeven om bij jou in Zweden intensief met je samen te mogen werken. Ik heb daar een fantastische en zeer leerzame tijd gehad, het was een ervaring die ik nooit zal vergeten.

Mijn promotor prof. dr. R. Sanderman. Beste Robbert, ik heb het erg gewaardeerd dat je vanuit de Medische Psychologie mijn promotor wilde zijn, dat je je hebt verdiept in de cardiologische onderwerpen van mijn proefschrift, en daar altijd vernieuwende inzichten vanuit je eigen vakgebied aan toe wist te voegen. Je hebt me geleerd om als onderzoeker bij het interpreteren van de data, de patiënt zelf niet uit het oog te verliezen. Ik wil je bedanken voor de altijd waardevolle bijdrage die je hebt geleverd aan mijn artikelen en aan mijn leerproces de afgelopen jaren.

De leden van de beoordelingscommissie, prof. dr. A.V. Ranchor, prof. dr. J.W.M.G. Widdershoven en prof. dr. H.B.M. van de Wiel, wil ik bedanken voor het doornemen van mijn proefschrift.

Alle co-auteurs van mijn artikelen wil ik bedanken voor hun bijdrage aan dit proefschrift.

Mijn collega's van de COACH groep wil ik bedanken voor de samenwerking en jullie feedback bij de (oefen)presentaties, het bespreken van de artikelen en natuurlijk de gezellige momenten tijdens teamuitjes, borrels en congressen! Martje,

Marie Louise en Ivonne, bedankt voor jullie expertise als teamleiders. Jullie zijn het COACH team van het eerste uur, en hebben alle 'ins' en 'outs' van het COACH tijdperk voor ons met ons gedeeld. Arjen, Imke, Maaike en Maurice, jullie zaten/zitten in het zelfde schuitje als ik, met dezelfde stress maar ook met dezelfde overwinningsmomenten, die we samen hebben kunnen vieren. Dank jullie allemaal voor de afgelopen jaren, zonder jullie was het niet zo leerzaam, maar vooral ook niet zo gezellig geweest.

Alma, ik wil je heel erg bedanken voor al je hulp tijdens, maar vooral ook in de laatste fase van het promotietraject. Jij wist mij altijd duidelijk te maken wat de volgende stap was, als ik door de bomen het bos niet meer zag. Audrey, ook bedankt voor jouw hulp.

Prof. dr. Hans Hillege en dr. Douwe Postmus wil ik bedanken voor de statistische ondersteuning. De mede promovendi op de 'eerste' wil ik bedanken voor de gezelligheid op de congressen. De collega's van cardio research wil ik bedanken voor de betrokkenheid en praatjes op de gang. In het bijzonder wil ik Margriet bedanken voor de gezelligheid tijdens onze ritjes naar de patiënten in heel Nederland, en de samenwerking bij het afnemen van de patiënten interviews en de dataverzameling voor het project over het bespreken van seksualiteit.

Familie en vrienden, ik wil jullie bedanken voor jullie oprechte belangstelling en interesse in mijn onderzoek, maar natuurlijk ook voor de gezellige momenten en jullie begrip en steun op de moeilijke momenten: Marrit, Jelmer, Theo, Wietske, Sylke, Yorrit, Brent, Joke, Gerda, Jacoba, Fiona, Joletta, Gillian, Jaap, Thessa, Petra, Wijnand, Rutger, Annemarie, Jeroen, Guido, Linda, Shelley, Corine, en natuurlijk mijn Twister vrienden; de maandag werd een dag om naar uit te kijken sinds ik met jullie theatersport: Eva, Gea, Geert Jan, Hanneke, Jan, Johan, Marianne, Mariano en Peter.

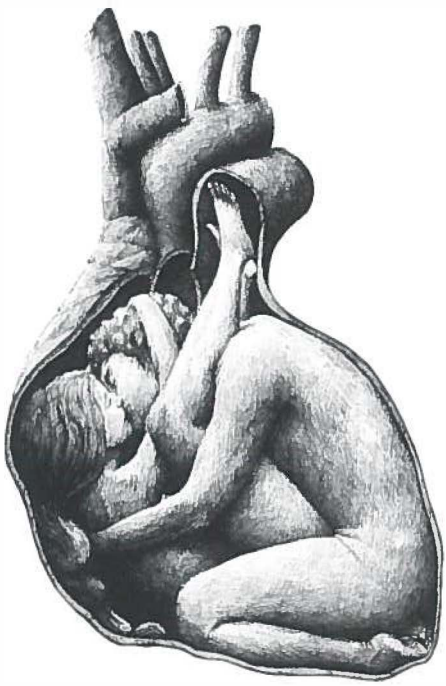
Mijn paranimfen Maurice Nieuwenhuis en Johan Pijlman. Beste Maurice, we zijn vrijwel gelijk begonnen met ons promotie traject bij de COACH groep, en sluiten het vrijwel gelijk af. Gedurende die periode ben je naast een collega en kamergenoot ook een goede vriend geworden. We hebben veel gedeeld, moeilijke en serieuze momenten, maar vooral ook veel geweldige momenten. We hebben veel gelachen, samen muziek gemaakt tot in de late uurtjes, en jij hebt me doen inzien dat voetbal meer is dan een spelletje, omdat je alle situaties in het leven met voetbal kunt vergelijken. Dank je wel voor een geweldige tijd!
Beste Johan, jij bent al sinds de vijfde klas van het VWO een goede vriend van mij. Nederlands, aardrijkskunde en economie werden ineens leuke vakken, omdat ik dan naast jou zat. We hebben veel gedeeld, destijds, maar ook alle jaren daarna. Na het VWO ging jij in Groningen studeren en ik in Leiden. We hebben altijd contact gehouden, en zagen elkaar weer wat vaker toen ik na jaren alsnog naar Groningen verhuisde. Maar ongeacht of het contact nou wel of niet intensief was, het was voor mij altijd vertrouwd. Dank je wel voor je jarenlange vriendschap!

Tenslotte, mijn ouders, leave heit en mem, tank jim wol foar jim leafde sûnder betingst. Jim haw altyd efter myn kar stien, en stean altyd klear foar my. Ik bin jim hiel tankber foar alles wit jim my haw jûn en bybrocht, en dat de doar nei jimme feiliche en waarme thús altyd iepen stiet.

Haren, oktober 2012

Tialda

Dankwoord NHS-COACH betrokkenen



Dankwoord NHS-COACH betrokkenen

De NHS-COACH studie (Nederlandse Hartstichting - Coordinating study on evaluating Outcomes of Advising and Counseling in Heart failure) is uitgevoerd in 17 ziekenhuizen in Nederland. Zonder de financiering van de Nederlandse Hartstichting en de grote inzet van velen was de COACH-studie niet tot stand gekomen, en had dit proefschrift er niet gelegen. Ten eerste wil ik het COACH onderzoeksteam (dr. Jochem Hogenhuis, dr. Ivonne Lesman-Leegte, dr. Marie Louise Luttik en dr. Martje van der Wal) en alle medewerkers van het Trial Coordination Center Groningen bedanken (waaronder prof. dr. Hans Hillege, dr. Nick Veeger en ing. Marco Assmann). Dankzij jullie inspanning is er een prachtige databank tot stand gekomen. Verder wil ik een ieder die in de centra heeft meegewerkt; hartfalenverpleegkundigen, cardiologen en interviewers, maar ook de medewerkers van de laboratoria en deelnemers aan het multidisciplinair overleg, langs deze weg hartelijk danken voor hun inzet:

Universitair Medisch Centrum Groningen
Hartfalenverpleegkundigen: drs. A. Koops, A. Klungel, K. van Dijk, G. Westra
Cardiologen: prof. dr. D.J. van Veldhuisen, prof. dr. A.A. Voors
Dataverzamelaars: G. Feringa, A. Schwencke, L. Grevink, K. Bruggink

Academisch Medisch Centrum, Amsterdam
Hartfalenverpleegkundigen: T. Veelenturf, R. Zwart, S. de Vries
Cardiologen/artsen: prof. dr. J.G.P. Tijssen, dr. W. Kok, dr. L.M. Konst, dr. J. van der sloot
Dataverzamelaars: L. IJzerman, R. Zuidervaart, E. Spoelstra, S. Stultiëns

Universitair Medisch Centrum St. Radbout, Nijmegen
Hartfalenverpleegkundigen: L. Knubben, L. Baltussen
Cardiologen: prof. dr. F. Verheugt, drs. L. Bellersen
Dataverzamelaars: J. de Natris, drs. L. Hogenhuis

Medisch Centrum Leeuwarden
Hartfalenverpleegkundigen: A. Obbema, A. Rijenga, D. van der Woude, J. de Bruin
Cardiologen: drs. C.J. de Vries, drs. R. Breedveld
Dataverzamelaars: A. Jonkman, C. Wassenaar

Twenteborg Ziekenhuis, Almelo
Hartfalenverpleegkundigen: E. Rodijk, M. Samsen, B. Beverdam, L. Bogemann
Cardioloog: dr. G.C.M. Linssen
Dataverzamelaars: H. Hondebrink, A. Disberg, M. Slaghekke

Atrium Medisch Centrum, Heerlen
Hartfalenverpleegkundigen: T. Thuis, I. Kremer, V. Post, S. Jongen
Cardioloog: dr. J.A. Kragten
Dataverzamelaars: drs. S. Hogenhuis, drs. E. Gaasbeek, drs. C. Beumer, B. Hoen

Jeroen Bosch Ziekenhuis, Den Bosch
Hartfalenverpleegkundigen: D. Jaftoran, V. van Zonsbeek, A. Berkhout
Cardioloog: dr. M.C.G. Daniëls
Dataverzamelaars: I. Samshuizen, D. Oosterkerk

Rijnstate Ziekenhuis, Arnhem
Hartfalenverpleegkundigen: drs. M. Rolfes, P. Nienaber
Cardioloog: dr. F.F. Willems
Dataverzamelaars: J. de Natris, M. Hubertus, drs. L. Hogenhuis, E. Eleveld

Amphia Ziekenhuis, Breda
Hartfalenverpleegkundigen: N. Creemer, I. Lauwerijssen, C. Paes
Cardioloog: dr. P.H.J.M. Dunselman
Dataverzamelaars: J. Hendriks, A. Lotstra, K. Terlaak

Refaja Ziekenhuis, Stadskanaal
Hartfalenverpleegkundigen: D. Thoma, R. Niewold, M. Wijbenga
Cardiologen: dr. L. van Wijk, Dr. K. de Vries
Dataverzamelaars: S. Vennik, drs. E. Prins

Tweesteden Ziekenhuis, Tilburg
Hartfalenverpleegkundigen: E. Hendriks, H. Broers
Cardioloog: prof. dr. J. Widdershoven
Dataverzamelaars: K. Janssen, B. de Kruijf, K. de Beer

Streekziekenhuis Midden Twente, Hengelo
Hartfalenverpleegkundigen: L. Odink, P. ter Horst, W. Wolters, L. Navis
Cardioloog: drs. A. Derks
Dataverzamelaars: J. Bijen, I. Horstman, A. Ottenhof, W. Bakker, B. Nijhuis

Scheper Ziekenhuis, Emmen
Hartfalenverpleegkundigen: A. Bakker, W. Veenstra, J.W. van Brakel
Cardioloog: dr. M.J. Nagelsmit
Dataverzamelaars: J. Kruimink, J. Pool, R. de Heus

Medisch Spectrum Twente, Enschede
Hartfalenverpleegkundigen: J. Roukema, H. Glazenburg, J. Grooters
Cardioloog: dr. P. van der Burgh
Dataverzamelaars: T. Meijer, H. Vroom, J. Poggenklas

Wilhelmina Ziekenhuis, Assen
Hartfalenverpleegkundigen: R. Aardema, J. Veninga
Cardioloog: dr. M.L. Pentinga
Dataverzamelaars: E. Tiemes, E. de Vos, N. van der Linden, E. Voois

Deventer Ziekenhuis, Deventer
Hartfalenverpleegkundigen: J. Burger, D. Pruijsers
Cardioloog: drs. D.J.A. Lok
Dataverzamelaars: L. Schoterman, M. van Buijsen, M. Scholten, H. Verheij

Oosterschelde Ziekenhuis, Goes
Hartfalenverpleegkundigen: J. Witkam, A. Roelse, E. Salawanei
Cardioloog: dr. A.H. Liem
Dataverzamelaars: A. Remijn, M. Franse, E. Wijs

Steeringcommittee
Prof. dr. D.J. van Veldhuisen (Voorzitter)
Prof. dr. T. Jaarsma
Dr. P.H.J.M. Dunselman
Prof. dr. W.H. van Gilst
Prof. dr. H.L. Hillege
Prof. dr. A.W. Hoes
Drs. D.J.A. Lok
Prof. dr. R. Sanderman
Dr. M.C.M. Senten
Dr. A. Speksnijder / Drs. I. Kamerling
Prof. dr. J.G.P. Tijssen

Eindpuntencommissie
Dr. C.M.H.B. Lucas (voorzitter)
Dr. J.H. Cornel
Dr. R.W.M.M. Jansen
Dr. F.H. Rutten
Dr. F. van den Berg

Bibliography

Bibliography

1. *Hoekstra T,* Jaarsma T, van Veldhuisen DJ, Hillege HL, Sanderman R, Lesman-Leegte I. Quality of life and survival in patients with heart failure. *Eur J Heart Fail* 2012; Accepted for publication.
2. *Hoekstra T,* Lesman-Leegte I, Luttik ML, Sanderman R, van Veldhuisen DJ, Jaarsma T. Sexual problems in elderly male and female patients with heart failure. *Heart* 2012; Accepted for publication.
3. *Hoekstra T,* Lesman-Leegte I, Couperus MF, Sanderman R, Jaarsma T. What keeps nurses from the sexual counseling of heart failure patients? *Heart Lung* 2012; **41**:492-499.
4. *Hoekstra T,* Jaarsma T, Sanderman R, van Veldhuisen DJ, Lesman-Leegte I. Perceived sexual difficulties and associated factors in patients with heart failure. *Am Heart J* 2012;**163**:246-251.
5. *Hoekstra T,* Lesman-Leegte I, van Veldhuisen DJ, Sanderman R, Jaarsma T. Quality of life is impaired similarly in heart failure patients with preserved and reduced ejection fraction. *Eur J Heart Fail* 2011;**13**:1013-1018.
6. *Hoekstra T,* Visser-Meily JMA, Kanselaar MA, Schouten RY, Jaarsma T. Is seksualiteit bespreekbaar in de CVA-zorg in revalidatiecentra? *NTR* 2011;**6**:5-9.
7. Jaarsma T, *Hoekstra T,* Schouten R, van Dooremaal M. *Bespreken van seksualiteit.* Den Haag: Hartstichting; 2011.
8. *Hoekstra T,* Lesman-Leegte I, van der Wal M, Luttik ML, Jaarsma T. Nurse-led interventions in heart failure care: Patient and nurse perspectives. *Eur J Cardiovasc Nurs* 2010;**9**:226-232.
9. *Hoekstra T,* Hanhart RJ, Lancel M. De crisiskaart in de forensische psychiatrie. *MGv* 2009;**10**:887-901.
10. Lancel M, *Hoekstra T,* Oosterbos N, de Jager B. Behandelbaarheid in het kader van terbeschikkingstelling met voorwaarden. *Sancties* 2009;**6**:325-337.
11. *T. Hoekstra.* 'Afwijkend' DNA speelt mogelijk een rol bij agressief gedrag. *GGZet Wetenschappelijk* 2009;**1**.

12. Meeter M, *Hoekstra T,* Klomps P, Borsboom D. *AMV, Amsterdamse Media Vragenlijst versie 2005. Public events test for retrograde amnesia.* Amsterdam: University of Amsterdam; 2005.

Curriculum Vitae

Curriculum Vitae

Tialda Hoekstra werd geboren op 23 november 1979 te Heerenveen. Ze is opgegroeid in Joure, en behaalde in 1999 haar VWO diploma aan het Bornego College te Heerenveen. Van 1999 tot 2001 studeerde zij Bio-farmaceutische Wetenschappen aan de Universiteit Leiden, en behaalde haar propedeuse. Vervolgens startte zij met de studie Psychologie aan de Universiteit Leiden. Binnen deze studie deed zij haar afstudeer onderzoek op de afdeling Neuropsychologie in het Leids Universitair Medisch Centrum, naar het ontwikkelen van een instrumentarium om amnesie na electro shock therapie bij depressie te meten. Haar praktijkstage liep ze op de afdeling Neuropsychologisch Onderzoek bij Parnassia te Den Haag. In januari 2006 behaalde zij haar doctoraal diploma met als afstudeertraject Neuropsychologie, binnen de afstudeerrichting Klinische- en Gezondheidspsychologie.

Na het afronden van de studie psychologie, bleef zij, aansluitend op haar praktijkstage, werkzaam als neuropsycholoog op de afdeling Neuropsychologisch Onderzoek bij Parnassia te Den Haag. Later dat jaar maakte zij de overstap naar de functie van onderzoeker bij de Divisie Forensische Psychiatrie van GGZ Drenthe te Assen. Hier bleef zij tot begin 2009 werkzaam, en verrichtte ze wetenschappelijk onderzoek naar onder andere de behandeleffecten van diverse behandelingen die binnen de Divisie werden aangeboden.

In februari 2009 werd zij als onderzoeker aangesteld op de afdeling Cardiologie van het Thoraxcentrum binnen het Universitair Medisch Centrum Groningen. Haar onderzoek was voornamelijk gericht op de kwaliteit van leven en seksuele problemen bij patiënten met hartfalen, met dit proefschrift als resultaat. Bij haar onderzoek maakte ze onder andere gebruik van de data van de COACH studie, welke door de Nederlandse Hartstichting werd gefinancierd.